ACUTE PURULENT MENINGITIS IN INFANCY AND CHILDHOOD WITH SPECIAL REFERENCE TO LATE MANIFESTATIONS.

BY

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C O N T E N T S

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INTRODUCTION.

In 1951 Trolle stated that the general impression in Infectious Diseases' Hospitals was that practically all the patients were discharged mentally normal. He went on to say that there had been some disagreement as to whether this was so or whether cerebrospinal meningitis might have left lasting mental sequelae.

Alexander (1952) reported that because of the widespread policy of using antibiotics for fevers of all causes and the growing tendency to use more than one therapeutic agent, pyogenic meningeal infections were seldom fatal. On the other hand, more children with cerebral damage were surviving.

Nelson (1959) wrote, "The decrease in mortality from purulent meningitis has been attended with a significant increase in permanent and serious neurological and mental sequelae. The reduction in them is one of the problems of the moment."

The purpose of this thesis is to see how a series of children in the North-East of Scotland suffering from purulent meningitis have fared. It is generally accepted that the mortality from all forms of purulent meningitis has fallen considerably since the pre-sulphonamide period. This may be due to earlier diagnosis and the institution of therapy with newer antibiotics and other

chemotherapeutic agents. Despite this happier outlook as to life and death, recent reports have shown that, although the grosser neurological defects are fewer, a considerable number of children are left with evidence of brain damage such as emotional instability, impaired memory, undue restlessness and inability to concentrate (Trolle, 1951). Because of these sequelae many children have been rendered ineducable at ordinary schools.

It was decided to see how the children in the present series had fared, and what sequelae they showed. Were they due to their illness entirely, or were there other factors such as environment and heredity playing a part? One way to tackle the problem was to ask specific questions as to his scholastic attainment where the patient was of school age. The school he attended was contacted and the schoolmaster was asked to report if the child was in a class for his own age and if progress was being maintained. A comment on his behaviour was requested and also whether there was any evidence of deafness. By asking these simple questions, it was thought that this would overcome the necessity of having to interview and assess all members of a family. This would have been very difficult to do, first because a large part of this study is retrospective, and second with the normal movement of families, contact with many would have been difficult. In an agricultural

area like the North-East of Scotland, many families make many moves, thus making follow-up difficult. The majority of the pre-school children have been seen personally, but in some instances the opinion of the family doctor has been obtained regarding the child's mental and physical status.

SECTION I.

MATERIAL

The period covered in this survey is from 1946 to 1961. No epidemics occurred during this time.

There were a total of 287 traced cases of whom 36 died and 251 survived. These cases were obtained by contacting the physicians in charge of infectious diseases for the counties of Aberdeen, Kincardine, Banff, and Moray, and also the island counties of Orkney and Shetland. The majority of patients were admitted to two centres in Aberdeen, the City Hospital and the Royal Hospital for Sick Children. This series includes all known cases of acute pyogenic meningitis occurring in the North-East of Scotland.

It was decided for this thesis to call the patients "Town" or "County" if their address on admission was Aberdeen Town or elsewhere in the area, respectively. This was done to see how the cases were distributed.

The distribution was "Town"- 185, and "County" cases - 102. Thus the incidence was almost 2:1 "Town" to "County", whereas the total population ratio is 1 town to 2 county.

The break-down of the types of meningitis in the "Town" cases was as follows: - Table 1.

It will be seen that of those who survived 168 cases occurred in urban dwellers and 83 in rural areas. This difference is the more significant as the division of the population is three times as heavy in the rural areas (Craig and Burrell 1950). There were over twice as many meningococcal and unidentified cases in the urban dwellers. The difference was not so marked in the pneumococcal and influenzal types, but there were more of each in town dwellers. Trolle (1951) found this difference in his series of meningococcal infection where most of his patients lived in the poorer, less well-housed areas of towns.

It was found necessary to call one of the types of meningitis "unidentified". The laboratory reports in many instances stated "purulent meningitis - presumably meningococcal although no organisms were seen on culture." However, certain marked differences were noted which showed that this "unidentified" type varied in certain instances from the proved meningococcal type e.g. the age distribution and seasonal incidence, the mortality rate and the incidence of late manifestations.

The age distribution showed a similarity in the over 12 months age group; there were 55 in the meningococcal group and 57 in the unidentified. In the under 12 month age group there was a marked difference. There were 71 in the meningococcal group and 26 in the unidentified group

TABLE 1.

	TOWN		COUNTY		TOTALS	
	Deaths	Recoveries	Deaths	Recoveries	Deaths	Recoveries.
Meningococcal	4	84	6	32	10	116
Unidentified	3	53	1	26	4	53
Influenzal	1	13	4	8	5	21
Pneumococcal	2	16	3	10	5	26
Mixed	3	2	1	3	4	5
Coliform	4	-	4	4	8	4
TOTALS	17	168	19	83	36	251
	185		102		287	

Comparing the seasonal incidence, there were 35 with 4 deaths in the meningococcal type and 33 with 4 deaths in the unidentified during the warmer months from June - November. There was a marked difference in the two types during the colder months from December - May. During these months there were 91 with 6 deaths in the meningococcal type and 50 with no deaths in the unidentified type. The mortality rate was higher in the meningococcal type where it was 7.8% as compared with 4.8% for the unidentified type.

The incidence of late manifestations was greater in the unidentified type being 18 of the 79 cases, an incidence of 40%. The corresponding figures for the meningococcal type being 12 of the 116 cases, an incidence of 27%

It has been suggested that the reason why no growth is obtained in the group now called unidentified is because of the widespread use of either penicillin or sulphonamide drugs prior to admission. Because the meningococcus is so sensitive to either of these drugs and such organisms as the staphylococcus and haem. influenzae are not, it has been presumed in the past that the offending organism was the meningococcus although no organism was seen on culture.

In view of the striking differences mentioned above

it was felt that this type could not be included with the meningococcal infections.

INCIDENCE OF TYPES OF MENINGITIS.

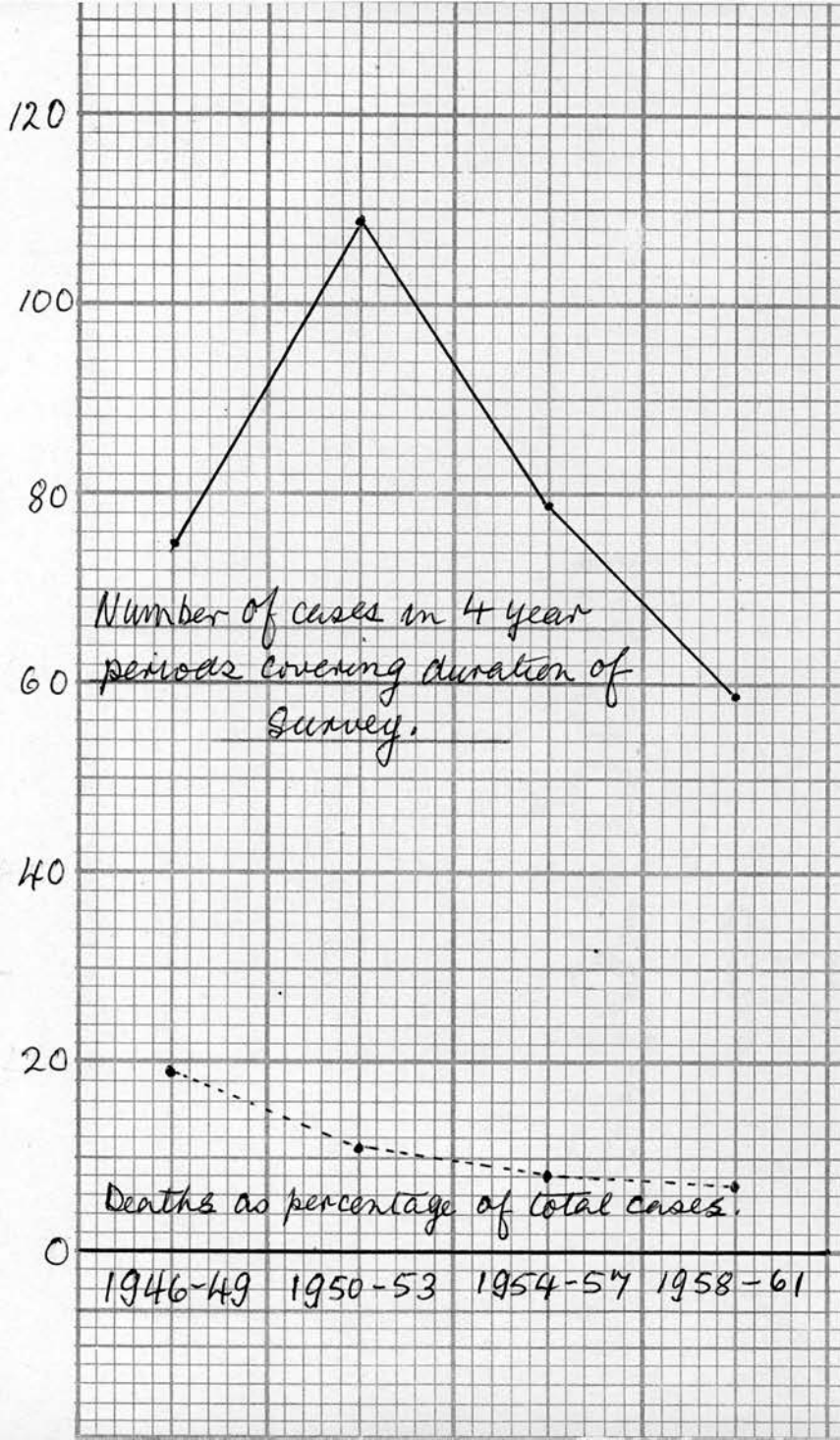
The figures for the years 1949 - 1961 are set out in the following table (Types of Meningitis). All cases of meningococcal meningitis were confirmed bacteriologically either by culturing the organism or seeing the organism in a smear or by blood culture. In the "unidentified" group cultures remained sterile. There were a few cases not falling into the four main groups; these have been classed as "mixed" and "coliform" respectively.

TABLE 2.

TYPES OF MENINGITIS

Year	Meningo	Unidentified	H.I.	Pneumo.	Mixed	Coliform	Totals	Recoveries	Dead
1946	9 (2)	12	3 (2)	2 (2)	-	-	26	20	6
1947	3	5 (1)	2	1 (1)	-	-	11	9	2
1948	4 (1)	2	-	2 (1)	1(1)	-	9	6	3
1949	6	1 (1)	3	2	-	3 (2)	15	12	3
1950	13	4	1	2	2 (1)	-	22	21	1
1951	14 (2)	11	3 (2)	3	-	1 (1)	32	27	5
1952	6 (1)	5 (1)	-	3	1 (1)	1 (1)	16	12	4
1953	14 (1)	10	-	3 (1)	-	-	27	25	2
1954	13 (1)	8	1	1	-	1 (1)	24	22	2
1955	8	3	1	3	1	-	16	16	-
1956	6	3.	2	1	-	3 (2)	15	13	2
1957	7	3	1	3	1 (1)	3 (1)	18	16	2
1958	10	7	4	-	2	-	23	23	-
1959	6 (1)	6	1	1	-	-	14	13	1
1960	6 (1)	2 (1)	2 (1)	1	-	-	11	8	3
1961	1	1	2	3	1	-	8	8	-
Totals	126(10)	83 (4)	26 (5)	31 (5)	9 (4)	12 (8)	287	251	36

(Deaths in Brackets)


120
100
80
60
40
20
0
Number of cases in 4 year periods covering duration of Survey.
Deaths as percentage of total cases.
1946-49
1950-53
1954-57
1958-61

It will be seen that meningococcal meningitis is the commonest type followed by unidentified. Pneumococcal infection was the third most common, then influenzal and finally coliform and mixed. As will be discussed later, this distribution of types of meningitis may have a bearing on the ultimate prognosis as far as intellect is concerned. The commonest type found in the United States is influenzal (Smith, 1954). It is in this type also that the highest incidence of late manifestations have been reported (Platou et al., 1959): in other series meningococcal infection has been the commonest (Hutchison and Kovacs, 1963).

When the totals for each 4 year period of this survey are totalled and plotted as a graph there appears to be a falling off in the number of cases. When the deaths are plotted as a percentage of total cases there is also a downward trend. The fall in total numbers may be due to better housing. The declining mortality reflects the earlier use of effective drugs.

Seasonal Incidence.

The seasonal incidence is set out in Table 3. It will be seen that meningitis of the four main types was commonest in the colder parts of the year - December - May - these months accounting for 185 (64%) of the total number. There were 102 (36%) cases during the period June - November.

TABLE 3. - UNIDENTIFIED MENINGITIS.

SEASONAL INCIDENCE.

TYPE	Jany	Feby	Mar.	Apr.	May	June	July	Aug	Sept	Oct.	Nov.	Dec.	Totals
Meningo	22	12	15(3)	11	18 (2)	9 (2)	4	7(1)	3	7	5(1)	13 (1)	126(10)
Purulent	9	7	7	9	12	6 (1)	9(1)	4(1)	4	6(1)	4	6	83(4)
H.I.	3	5(1)	2(1)	2	4(2)	3 (1)	1	1	2	-	1	2	26(5)
Pneumo.	3	5(1)	4(2)	1	1	2	5	2	1	2	3(1)	2(1)	31(5)
Mixed	2(1)	1	-	3(2)	-	-	-	-	1	-	2(1)	-	9 (4)
Coliform	-	1(1)	1(1)	2(2)	-	2(2)	2(1)	2	1	-	1(1)	-	12) 8)
Totals	39(1)	31(3)	29(7)	28(4)	35(4)	22(6)	21(2)	15(2)	13	15(1)	16(4)	23(2)	287 (36)

(Deaths in Brackets)

December	-	May	185	(21)
June	-	November	102	(15)
Totals			287	(36)

Banks (1949) stated that in non-epidemic years the number of cases occurring in the first half of each year was approximately twice that of the second half of the year. Trolle (1951) reported that the colder and wetter months gave the highest incidence in his series. In Rantsalo and Kauhtio's (1958) series, 61% occurred between November and April; 39% occurred between May and October. Kneebone (1961) commented that most of his cases occurred in the colder weather.

In the present series there is not such a marked difference, but in meningococcal infection 91 of the cases occurred in the colder months of the year and 35 in the warmer months.

There were 36 deaths, 21 occurred during the colder part of the year and 15 during the remainder.

Sex Incidence.

The sex distribution of this series of 287 showed 163 males and 124 females, an incidence of 1.2: 1. Joe (1947) stated that males are more often affected than females. Banks (1949) wrote, "Sex has no influence per se, but, in practice, the propertiens of males to females is about 3:2. This is associated with the greater degree of exposure to infection of males during their occupation in peace and war, and in infancy to the greater proportion of males in the population." Of Rantsalo and Kauhtio's (1958) series 257 cases, 142 were boys and 115 were girls.

The distribution in the present series is in keeping with the findings reported above.

TABLE 4

AGE INCIDENCE (Deaths in brackets)

TYPE	0-3 mths	3-6 mths	6-12 mths	1 - 3 yrs	3 - 5 yrs	5 - 12 yrs	Over 12 yrs	Totals
Meningo	10 (5)	22 (2)	39 (1)	28	16 (2)	11		126 (10)
Unidentified	1 (1)	9 (1)	16 (2)	23	15	18	1	83 (4)
H.I.		1 (1)	10 (2)	10	4 (2)	1		26 (5)
Pneumo.	4 (2)	2	5	8 (2)		12 (1)		31 (5)
Mixed	1 (1)		2	2 (2)	3	1 (1)		9 (4)
Coliform	9 (5)	3 (3)						12 (8)
Totals	25 (14)	37 (7)	72 (5)	71 (4)	38 (4)	43 (2)	1	287 (36)
	134 (26)			153 (10)				

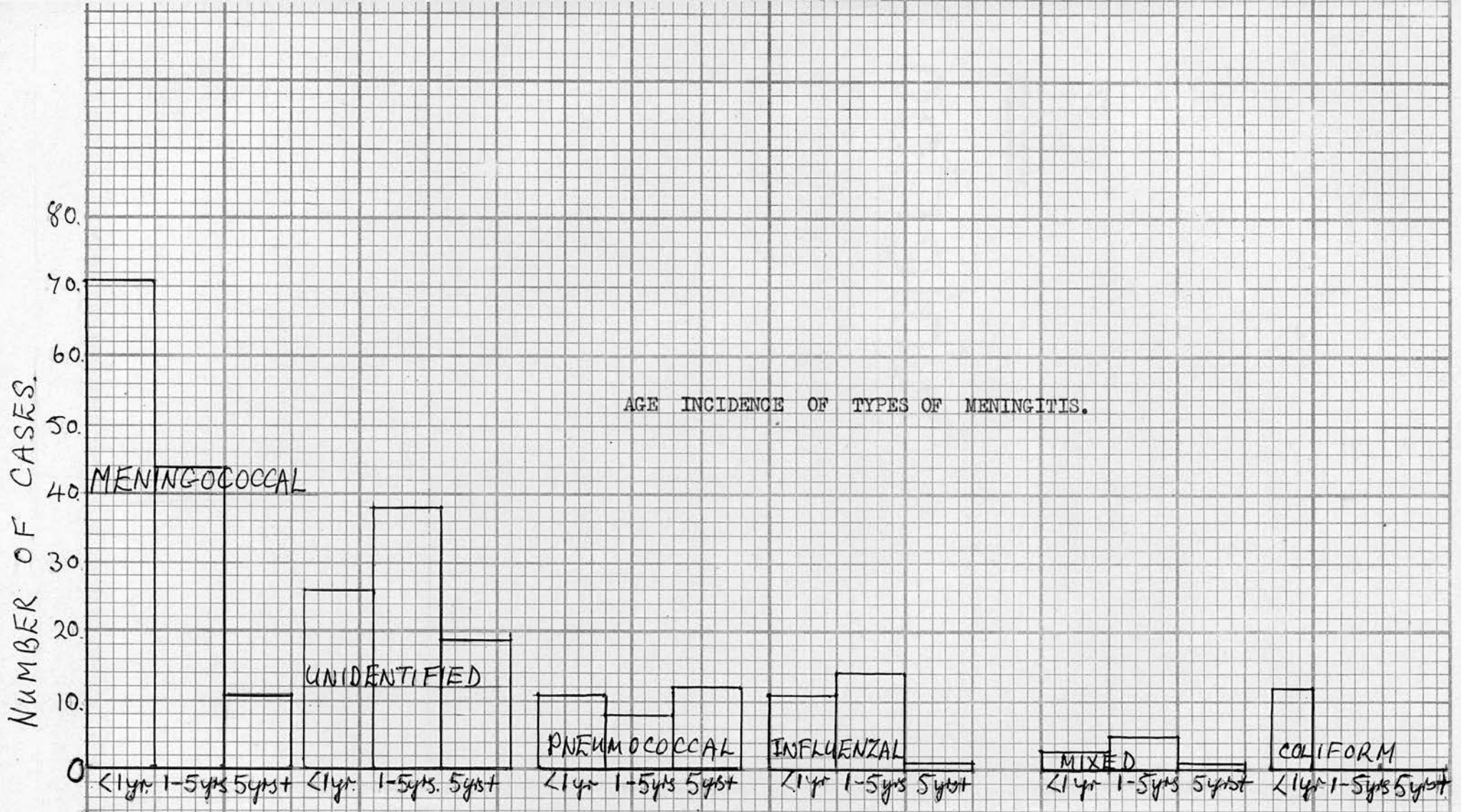
AGE INCIDENCE.

The age incidence is shown in Table 4 and accompanying graph.

In the total series of 287 there were 134 (47%) under the age of 1 year, 109 (31%) between the age of 1 and 5 years and 44 (15%) over the age of 5 years. This agreed with the known incidence of septic meningitis of all types. (McKendrick 1954). Of the 126 cases of meningococcal infection 71 (56%) occurred under the age of 1 year. There were 83 in the unidentified group and 38 (46%) occurred between the age of 1 and 5 years. A similar distribution was found in the influenzal group where 14 (53%) of the 26 patients were in the age group 1 to 5 years.

The peak incidence in the pneumococcal cases was in the over 5 years age group. There was a total of 31 cases and 12 (39%) were in this age group. All the 12 cases in the coliform group occurred under the age of 1 year.

Joe (1947) reported that the chief prevalence is in children under 5 years of age. Banks (1949) gave the following figures:- about half the cases occurred under the age of 5 years, and as many as 65% under the age of 10 years. Rantaalo and Kauhtio (1958) found that 66% of their patients became ill in the first year of life. In Kneebone's (1961) series, 87% were under the age of


AGE INCIDENCE OF TYPES OF MENINGITIS.
NUMBER OF CASES.
80.
70.
60.
50.
40.
30.
20.
10.
0
MENINGOCOCCAL
UNIDENTIFIED
PNEUMOCOCCAL
INFLUENZAL
MIXED
COLIFORM
<1yr. 1-5yrs 5yrs+

4 years and more than half were under 1 year. Hutchison and Kovacs (1963) found that 55% of their patients were under 12 months when they developed acute purulent meningitis.

The age distribution of the present series is in keeping with these results. The one exception was the pneumococcal group where the peak incidence was in the child of school age.

Of the 36 deaths in the present series, 34 occurred under the age of 5 years. There were 30 deaths under the age of 3 years, 26 (72%) under the age of 12 months, 21 (58%) under the age of 6 months and 14 (38%) under the age of 3 months. The peak incidence was in the under - 12 months age group. In Trolle's (1951) series, more than half the deaths occurred in infents under the age of 12 months. Kneebone (1961) reported an incidence of 75%, and Hutchison and Kovacs (1963) found that all their deaths were under the age of 12 months.

Thus the age incidence of the deaths in the present series was in keeping with the figures reported above.

Symptoms and Signs.

An analysis of the symptoms and signs is recorded in the following tables:-

TABLE 5 - TOTAL FIGURES.

Symptoms and Signs	Number affected	Percentage
Fever	268	93
Neck Stiffness	247	91
Vomiting	235	81
Irritability	159	55
Anorexia	140	48
Kernigs	139	48
Drowsiness	119	44
Pallor	109	37
Rash	93	32
Headache	77	26
Bulging fontanelle	79	26
Coma	49	17
Vacant Look	49	17
Convulsions	42	15
Squint	22	7
Symptomless	1	0.3

TABLE 6 - SURVIVALS.

Symptoms and Signs	Number affected	Percentage
Fever	233	92
Neck stiffness	226	90
Vomiting	213	82
Irritability	142	56
Kernigs	121	48
Anorexia	120	47
Drowsiness	111	44
Pallor	99	39
Rash	79	31
Headache	72	28
Bulging Fontanelle	66	26
Vacant Look	47	18
Coma	36	14
Convulsions	27	10
Squint	20	7
Symptomless	1	0.3

TABLE 7 - DEATHS.

Symptoms and Signs	Number affected	Percentage
Fever	34	94
Vomiting	22	61
Neck stiffness	21	58
Anorexia	20	55
Irritability	16	44
Convulsions	15	42
Coma	15	42
Pallor	11	30
Rash	14	38
Bulging Fontanelle	13	36
Kernigs	7	19
Drowsiness	8	25
Headache	5	13
Vacant Look	2	5
Squint	2	5

It will be seen that the commonest symptoms were vomiting, irritability, anorexia, drowsiness, coma and convulsions. The commonest signs were fever, neck stiffness, positive Kernig's sign, rash and bulging fontanelle. The main difference was in the marked increase in convulsions and coma in these patients who died. This may indicate a more severe infection.

Hawarth (1953) commenting on the high case mortality in bacterial meningitis, stated that one of the factors causing this was the delay in reaching a diagnosis. He stated that classical features such as stiffness of neck and spine and also Brudzinski's and Kernig's signs were often absent. Increased pressure in fontanelle often was not present, especially where dehydration was present. In his series of 50 cases under the age of 12 months, the chief symptoms and frequencies were vomiting in 62%, irritability in 56%, anorexia in 32%, drowsiness in 18%, and convulsions in 10%. The chief physical signs were neck stiffness in 62%, tense or bulging fontanelle in 44%, positive Kernig's sign in 26% and vacant look or squint in 12%. Trolle (1951) and Kneebone (1961) described similar signs and symptoms. It will be seen that there was a marked difference in the incidence of convulsions and coma in those who survived and those who died. In the survivors, coma occurred in 14% and convulsions in 10%. The corresponding figures for those who died were 42% and 42%

McKendrick (1954) found an incidence of coma of 24% in his series suffering from meningococcal infection. The figures for pneumococcal and influenzal meningitis were 50% and 17.5% respectively.

Trolle (1951) reported convulsions in 15% of his series, and Rantsalo and Kauhtio (1958) gave a figure of 33%. Kneebone (1961), on the other hand, stated that "convulsions were surprisingly infrequent but more frequent in influenzal".

It was decided to study the effect of convulsions and coma on the outcome of those who survived. Presumably those admitted in convulsions or coma were suffering from a severe infection. The result of this study is reported later (p. 121).

DEATHS.

Alexander (1948) pointed out the striking fall in the mortality rate in purulent meningitis. She stated that up to 1936 meningococcal meningitis was the only one of the meninigitides in which recovery might be anticipated with any regularity; that pneumococcal and haemophilis influenzae meningitis were almost universally fatal, the mortality in infants and children under 3 years being virtually 100%; and recovery was rare from meningitis caused by streptococcus haemolyticus, staphylococcus, and Gram-negative bacilli of intestinal origin.

Some of the reported figures of mortality rates showed considerable fluctuation; McKendrick (1954) 6.6%; Desmitt (1955) 6.1%; Kauhtio and Rantsalo (1958) 33% Platou et al. (1959) 12.9%; Kneebone (1961) 17.3%; Hutchison and Kovacs (1963) 9.8%

There were 36 deaths in the series of 287 (12.5%).

The following table shows death rates in the main types of purulent meningitis discussed in this thesis.

TABLE 8.

TYPES	Total Patients	Deaths	Percentage
Meningococcal	126	10	7.8
Unidentified	83	4	4.8
H.I.	26	5	19.2
Pneumococcal	31	5	16.1
Mixed	9	4	44.4
E. coli	12	8	66.6
Totals	287	36	

There were 10 deaths due to meningococcal meningitis, an incidence of 7.8% as shown in Table 8. This compares with other published figures; Banks (1951) 7.3%; Desmitt (1955) 11.6%; Kneebone (1961) 8.2%, and Hutchison and Kovacs (1963) 6.1%.

Trolle (1951) divided the mortality rates of his series into three eras: (1) from 1920 - chemotherapy era, the fatality rate was 65.8%; (2) chemotherapy - 1940, when it fell to 33.3%, and (3) from 1940 - 1945, when the fatality rate dropped to 11.9%

It will be seen from Table 9 that 5 infants died under the age of 3 months, 2 between the age of 3 and 6 months, 1 between the age of 6 and 12 months, and 2 in the age group 3 - 6 years. Thus, 8 of the 10 deaths in this group were under the age of 1 year, in keeping with the findings of other writers (Kneebone, 1961); Hutchison and Kovacs, 1963)

The duration of symptoms prior to admission was short, being between 12 and 24 hours in 8, the others being 96 and 168 hours respectively. The presenting symptoms were similar to those patients who recovered and were fever, bulging fontanelle, neck stiffness and vomiting. In 3 cases only was a petechial rash present.

Four patients were admitted in coma and 2 of those also had convulsions.

The time till death after admission was under 12 hours in 6, under 24 hours in 2, 46 hours and 72 hours respectively. Thus, 8 of the 10 patients died in less than 24 hours of being admitted.

TABLE 9

DEATHS - MENINGOCOCCAL

Year	Type of Meningitis	Age	Duration of Symptoms	Presenting Symptoms	Time till death after Admission	PENICILLIN. I.T.	PENICILLIN. I.M.	Sulpha	Others	Steroids	Post-Mortem.
1946	Meningo	3/12	24hrs	F.,B.F.,N.S., A.	24 hrs	50,000	0.1M	1.0G			No P.M.
1946	Meningo	4 yrs	24 hrs	F.,V.,pallor coma & convuls	12 hrs	50,000	0.1M	1.0G			No W.-F. syndrome
1948	Meningo	6/12	168 hrs	F.,V.,I.,A.	72 hrs	50,000 20,000x2	0.25M	4.5G			No W.-F. syndrome
1951	Meningo	4/52	24hrs	R.,B.F.,V., pallor	24 hrs			1.25G			No P.M.
1951	Meningo	9/12	96hrs	N.S.,V., pallor	46 hrs	10,000	0.1M	0.75G		Eucortone	Thrombosis Sup.Sag.Sinus.
1952	Meningo	1/52	24 hrs	A.,collapse	3 hrs		0.1M		Strepto 0.6G		No W.-F. syndrome.
1953	Meningo	5/52	24 hrs	B.F.,A.,D., pallor	12 hr	20,000	6.0M			Cortisone 25 mgm	Bilateral Adrenal Haemorrhages
1954	Meningo	3yrs 9mths	24 hrs	R.,coma	10 mins						Superficial Haem. R. suprarenal
1959	Meningo	9/52	12 hrs	F.,B.F.,V., pallor,coma & convuls	12 hrs	10,000	1.0M	0.5G		Cortisone 100 mgms	No W.-F. syndrome
1960	Meningo	5/12	12 hrs	F.,R.,B.F., N.S. coma	2 hrs		1.5M	0.5G	Strepto 0.5G	Cortisone 100 mgm	No P.M.

F = Fever; R = Rash; V = Vomiting; I = Irritability; N.S. = Neck stiffness
B.F. = Bulging Fontanelle; A = Anorexia; D = Drowsiness.

Treatment under these circumstances was of short duration and was thus inadequate. Three of the patients had steroid therapy and a fourth had Eucortone.

Post-mortem examinations were carried out in 7 of the patients. In one only was there adrenal haemorrhage, no such haemorrhages were found in 4, 1 other had a superficial haemorrhage in one adrenal gland and the other had thrombosis of the superior sagittal sinus. Of the 3 patients exhibiting petechiae, no post-mortem examination was held on 2, and the third patient showed a superficial haemorrhage in one adrenal gland. The one patient who did show haemorrhage in the adrenal gland did not have a petechial rash.

COMMENT:

It would appear that these patients suffered from an overwhelming meningococcal infection, death ensuing before adequate therapy could be exhibited. It is interesting that of 3 patients with petechial rashes, in the one post mortem examination carried out no evidence of adrenal haemorrhage was found. Conversely, in the post-mortem where haemorrhage of the adrenal gland was found, the patient in life showed no petechial rash.

TABLE 10

DEATHS - UNIDENTIFIED

Year	Type of Meningitis	Age yrs	Duration of Symptoms	Presenting Symptoms	Time till Death after Admission	Penicillin I.T.	Penicillin I.M.	Sulpha	Others	Steroids	Post Mortem
1947	Unid,	7/52	168 hrs	F.,I.,A. convulsions	47 days	Several courses of Penicillin		Several courses			Cerebral Abscess
1949	Unid.	10/12	24 hrs	F.,R.,V., I.,pallor	24 hrs		0.1G			Eucortone	Adrenals-Oedema of cortex & Absence of lipoid granules
1952	Unid	10/12	168 hrs	F.,N.S.,V.,I., A.,D.,convulsions.	12 hrs	30,000					Sinus Thrombosis.
1960	Unid.	6/12	24 hrs	F.,R.,B.F., I.,A.	72 hrs		2.0M		Chloromycetin 750 mg.	Cortisone 100,75 50	Oedema round adrenals but no Haemorrhages

F = Fever; R = Rash; V = Vomiting; I = Irritability; N.S.= Neck stiffness; A = Anorexia
D = Drowsiness.

DEATHS - "Unidentified"

In this type of meningitis there were 4 deaths, all under the age of 1 year, an incidence of 4.8%. Kneebone (1961) found a mortality of 5.4% in his series and Hutchison and Kovacs (1963) an incidence of 4.0%.

One was aged 7 weeks, a second 6 months, and the other 2 were 10 months old at the time of admission. (See Table 10.)

The duration of symptoms prior to admission was short in 2, being 24 hours; in the other 2 patients it was much longer, being 7 days in each.

The presenting symptoms were fever, irritability and anorexia. Neck stiffness and bulging fontanelle occurred in 2 of the 4 patients. Convulsions were a presenting feature in 2 of the cases. The time till death after admission was 12 hours, 24 hours, 72 hours and 47 days respectively. Thus, treatment was of very short duration in 2 because death occurred so quickly. One patient had Eucortone and another Cortisone. These were the two patients who had petechial rashes.

Post-mortem examinations were carried out in all 4 cases. In none was frank haemorrhage of the adrenals found. In 2, the adrenal cortex was oedematous and in one of these lipoid granules were

TABLE 11

DEATHS - INFLUENZAL

Year	Type of Meningitis	Age yrs	Duration of Symptoms	Presenting Symptoms	Time till death after admission	PENICILLIN. I.T.	PENICILLIN. I.M.	Sulpha	Others	Steroids	Post Mortem
1946	Infl.	11/12	336 hrs	N.S.,I.,K.	54 days	Several prolonged courses					No.
1946	Infl	14/52	168 hrs	F.,I., convulsions	17 days	20,000 x 3	0.05M x 17	17.0G			No. W.-F. Syndrome
1951	Infl	3yrs 2mths	120 hrs	F.,R.,N.S., V.,I.,K.	3 hours 40 mins.	10,000					No.
1951	Infl.	3½ yrs	48 hrs	F.,N.S.,V., I.,K.,coma & convuls.	72 hrs	20,000 x 3	1.8M	14.5G.	Streptomyc. 0.05 x 3 I.T. 0.6 x 3 I.M.		No.
1960	Infl	9/12	48 hrs	N.S.,V., coma	<24 hrs	10,000			Chloro Cortmycetin isone 1.0G		No. W.-F. Syndrome

F = Fever; R= Rash; V = Vomiting; I = Irritability; N.S. = Neck Stiffness; A = Anorexia
K = Kernig's sign; D = Drowsiness.

absent. It was these two patients who had petechial rashes. Another patient had thrombosis of the superior sagittal sinus and the other had a cerebral abscess. It was this last patient who survived for 47 days.

COMMENT:

The age of all 4 deaths was under 1 year. None of the patients with petechial rashes showed adrenal haemorrhage. In 2 of the 4 cases, the presenting symptoms were not particularly referable to the central nervous system.

DEATHS - Influenzal.

Table 11 sets out the findings of the deaths from influenzal meningitis patients of whom there were 5, an incidence of 19.2%. This figure is much higher than in some reported series (Platou et al., 1959, 7.5%; Hutchison and Kovacs, 1963, 5.2%; McKendrick, 1954, 6%).

Since the institution of therapy with streptomycin, and later chloramphenicol, to both of which H. influenzae organisms are sensitive, there has been 1 death in 14 patients so treated. This would give a mortality figure of 7.1%, which is in keeping with the above quoted results.

There were 3 patients under the age of 11 month, the other 2 were under the age of 3 years and 6 months.

the other 2 were under the age of 3 years and 6 months.

The duration of symptoms before admission was 48 hours in 2, 120 hours in a third, 168 hours in a fourth, and the fifth had symptoms for 336 hours prior to admission.

Of the common symptoms, fever, neck stiffness and irritability were the most frequent findings. Irritability was a striking feature. One patient had a petechial rash. One was admitted in coma, a second had convulsions and a third convulsions and coma.

Death ensued in 3 hours 40 minutes, less than 24 hours, 72 hours, 17 days and 54 days respectively.

Therapy was considered to be inadequate in 4 of the patients; in 2 of these the time factor was too short for the drugs used to be effective; in the two others the drugs used had little or no effect as the organism was not sensitive to them. In the remaining patient, treatment again was not of sufficient duration. Post-mortem examination was allowed in two cases only, and no evidence of suprarenal haemorrhage was found.

COMMENT:

The age at death in this type of infection was older than in meningococcal or unidentified type meningitis, although 3 of the 5 were under 1 year. The presence

The presence of coma or convulsions would appear to have a bad prognosis.

The use of effective drug therapy markedly reduced the mortality rate.

DEATHS - Pneumococcal

There were 5 deaths from pneumococcal meningitis, a fatality rate of 16.1%. Details are shown in Table 12. Similar figures were published by Rantsalo and Kauhtie (1958) 19.0%; Kneebone (1961) gave a figure of 27.8%.

Of the 5 patients who died from pneumococcal meningitis, the respective ages were 1 month, 9 weeks, 1 year and 2 months, 2 years and 6 months, and 8 years.

The duration of symptoms prior to admission were 48 hours, 120 hours, 72 hours, 72 hours and ? 21 days.

Of the common symptoms, fever, coma, vomiting, neck stiffness, and irritability were the most frequent findings. No patient had a petechial rash.

Death ensued in 60 hours, less than 48 hours, 28 hours, 4 hours and 30 minutes, and less than 12 hours after admission.

In at least 2 of these patients treatment was of

TABLE 12

DEATHS - PNEUMOCOCCAL

Year	Type of Meningitis	Age yrs	Duration of Symptoms	Presenting Symptoms	Time till death after Admission	PENICILLIN. I.T.	PENICILLIN. I.M.	Sulpha	Others	Steroids	Post Mortem
1946	Pneumo	$2\frac{1}{2}$	72 hrs	F.,N.S.,V., I.,D.,coma	$4\frac{1}{2}$ hrs	20,000	0.2M	2.0G			No. W.-F Syndrome
1946	Pneumo	9/52	120 hrs	B.F.,V., pallor	< 48 hrs	40,000	0.5G	1.0G			No. W.-F. Syndrome
1947	Pneumo	1/12	48 hrs	F.,coma & convulsions	60 hrs		1.35M	3.5G			No.
1948	Pneumo	14/12	72 hrs	F.,V.,semi-coma	28 hrs	10,000	0.3M	3.0G			No.
1953	Pneumo	8	?21 dys	F.,N.S.,I.,D.,headache	<12 hrs	20,000	2.0M	1.0G		Cortisone 50 mg.	No. W.-F. Syndrome

F = Fever; V = Vomiting; I = Irritability; N.S. = Neck Stiffness; A = Anorexia; D = Drowsiness

such short duration that it must be considered ineffective because of the speed with which death resulted. In the other 3 the dosage of drugs used will be seen to be very small and, for this reason, also inadequate. Since starting the routine described under treatment (p. 100), there has been 1 death in 18 patients - a mortality rate of 5.5%. This is in keeping with other reported series (McKendrick, 1954, 7%: Platou et al. 1959, 8.8%; Hutchison and Kovacs, 1963, 10.5%)

Post-mortem examinations were allowed in 3, and in none of these was adrenal haemorrhage found.

COMMENT:

The most significant feature in this type of meningitis is the occurrence of coma in 3 of the fatal cases. Two of the deaths were under the age of 3 months, the other 3 deaths were aged 1 year and 2 months, 2 years and 6 months, and 8 years respectively.

DEATHS - Mixed

There were 4 deaths in the group called "Mixed", an incidence of 44.4%. There were 3 cases of meningococcal septicaemia, and one of staphylococcal meningitis. The details are shown in Table 13.

In the 3 cases with meningococcal septicaemia the

TABLE 13

DEATHS - MIXED

Year	Type of Meningitis	Age yrs	Duration of Symptoms	Presenting Symptoms	Time till death after Admission	PENICILLIN. I.T.	PENICILLIN. I.M.	Sulpha	Others	Steroids	Post Mortem
1948	Meningo Septic.	9	<12 hrs	F.,R.,N.S., V.,K.,D.,	12 hrs		I.M. (IV)	2G (IV)		Eucortone	W.-F. Syndrome
1950	Meningo Septic	2	<24 hrs	F.,R.,N.S., V.,I.A.	1 hr 40 mins						W.-F. Syndrome
1952	Meningo Septic	17 mths	<24 hrs	F.,R.,N.S., V.,D.	7 hrs		0.2M				W.-F. Syndrome
1957	Staph. Aureus	9/52	?several days ? 10	A. Convulsions	53 days	Streptomycin, Erythromycon	Chloromycetin			Cortisone	Basal Block.

F = Fever; R = Rash; N.S. = Neck stiffness; V = Vomiting; K = Ke nig's sign; D = Drowsiness
I = Irritability; A = Anorexia.

ages were 17 months, 2 years and 9 years respectively. The duration of symptoms was very short and was less than 12 hours in one and less than 24 hours in the other two patients.

The commonest presenting symptoms were fever, rash, neck stiffness and vomiting; one was comatose and one other was convulsing on admission. Death ensued in under 24 hours in all, the times being 1 hour 40 minutes, 7 hours and 12 hours respectively.

Treatment was commenced in 2 cases, but owing to the rapidly fatal outcome all the patients died before effective therapy could be administered. One patient was treated with Eucortone.

The 3 patients with meningococcal septicaemia had bilateral adrenal haemorrhages at post-mortem examination.

The patients with staphylococcal infection had a longer period before admission, and although the exact time could not be estimated, this was probably 10 days. Despite repeated courses of therapy, this patient died 53 days after admission.

Post-mortem examination in the staphylococcal case showed a basal block due to adhesions.

COMMENT:

Thus it would seem that in the meningococcal septicaemia cases, the patients were overwhelmed and died before adequate therapy could be instituted. In the patients with staphylococcal infection, onset was more insidious and perhaps the meningitis had been present for several days prior to admission. The delay in instituting therapy might be the reason why this patient failed to respond to adequate therapy.

In the 4 patients in the group, 1 was admitted with convulsions and 1 was comatose. Thus convulsions and coma on admission were very bad prognostic signs as far as death is concerned (see also chapter on "Sequelae").

All the 3 patients with meningococcal septicaemia showed a petechial rash and at post-mortem the classical finding of the Waterhouse-Friderichsen syndrome. The suprarenal glands were completely destroyed by haemorrhage.

DEATHS - "Coliform Group"

In the "coliform group" there were 8 deaths, an incidence of 66.6%. This is in keeping with other published figures: Smith (1954) reported an incidence of 71% and Dyggve (1962) an incidence of 56% Of the 8 deaths, 6 were due to coliform organisms, 1 to

"paracolon bacillus" and 1 to infection with salmonella thomson. The details are included in Table 14.

The ages on admission varied from 2 days to twelve weeks.

With two exceptions the duration of symptoms was under 24 hours. In the remaining patients it was probably 6 days and 14 days respectively.

The presenting symptoms in the 8 who died were in order of frequency - fever in 8, anorexia in 5, bulging fontanelle in 5 and vomiting in 2. Irritability was present in 2 and another 2 were convulsing. Two patients had meningomyeloceles on admission, and 2 others subsequently developed hydrocephalus. These 2 patients were in hospital for 4 weeks and 14 weeks respectively before death ensued. Death occurred in the other 6 patients in 1 day, 3 days, 5 days, 6 days, 7 days, and 45 days respectively.

Treatment was thus of short duration in 5 patients. Death occurred in 2 within 24 hours of commencing treatment, 1 had no drug therapy, and in 2 other patients death occurred within 5 days and 7 days respectively. Those 2 patients were treated with tetracycline and streptomycin. In the 2 who developed hydrocephalus, treatment of longer duration was possible; one had penicillin,

chloromycetin and streptomycin, the other had aureomycin, chloromycetin and streptomycin. The patient with salmonella thomson infection survived for 45 days and had repeated courses of penicillin, streptomycin, chloromycetin and sulphadiazine.

Post-mortem examination was carried out in 5 of the 8. The patient with paracolon bacillus infection showed bilateral adrenal haemorrhages. In life this patient had no petechial haemorrhages into the skin.

COMMENT:

Dyggve (1962) pointed out that the symptoms were generally vague and undiagnostic; 6 only of his 20 patients had signs referable to the central nervous system. In the present series 5 of the 8 patients had signs of central nervous system involvement. Another feature was the short duration of symptoms prior to admission - 6 of the 8 were of less than 24 hours.

Incidence of petechial rash during life and relationship to adrenal haemorrhage found at post-mortem.

One of the deaths from influenzal meningitis had a petechial rash and in the two post-mortems carried out no suprarenal haemorrhage was found. No frank adrenal haemorrhages were found in the deaths from unidentified type meningitis, but two had a petechial rash.

TABLE 14

DEATHS - COLIFORM

Year	Type of Meningitis	Age yrs	Duration of Symptoms	Presenting Symptoms	Time till death after admission	Treatment	Others	Steroids	Post Mortem
1949	E.Coli	5/52	23 hrs	F.,B.F.,N.S. V.,I.	5 days	Streptomycin I.T.I.M. 20mgm.40mgm x 6			Purulent Meningitis
1949	E.Coli	2/365	24 hrs	F.,V.,A.	3 days	Oral Penicillin			Acute Meningitis
1951	E.Coli	3/52	?6dys	F.,B.F.,A.	4 wks	Aureomycin Chloromycetin, Streptomycin.			No. P.M. Hydrocephalus.
1952	E.Coli	4/365	24 hrs	F.,I.,A.	14 wks	Penicillin Streptomycin Chloromycetin			Hydrocephalus.
1954	Sal. Thom.	3/12	?14dys	F.,B.F.,A. convulsions	45 days	Repeated courses of Penicillin, streptomycin, chloromycetin sulpha.		Cortisone terminally	No. P.M.
1956	E.Coli	3/52	24 hrs	F.,B.F.,M.	7 days	Terramycin			Purulent Meningitis
1956	E.Coli	9/52	24 hrs	F.,M.	6 days				No.P.M.
1957	Para ColonB	6/365	24 hrs	F.,B.F.,N.S., A.,Convuls	1 day	Penicillin& streptomycin			Adrenal Haemorrhages.

F = Fever; B.F. = Bulging fontanelle; N.S. = Neck Stiffness; V = Vomiting;
I = Irritability; A = Anorexia, M = Meningomyocele.

None of the pneumococcal deaths had a rash and no suprarenal haemorrhages were found at the three post-mortems.

Of the 10 patients dying from meningococcal meningitis, 3 had a petechial rash. Unfortunately, no post-mortem was allowed in 2 of those and in the other, one suprarenal showed slight haemorrhage. In all, there were 7 post-mortem examinations, and one of these showed bilateral adrenal haemorrhage. This patient did not have a petechial rash.

In the deaths from the mixed type of meningitis, the three patients with meningococcal septicaemia all had petechial rashes and at post-mortem all showed the typical Waterhouse-Friderichsen syndrome.

Of the "coliform" deaths, the patient with 'paracolon bacillus' meningitis showed adrenal haemorrhage at post mortem, but exhibited no petechial rash in life.

It would seem, therefore, that the mere presence of a petechial rash during the course of meningitis does not justify diagnosing adrenal haemorrhage.

Meningococcal infections frequently have petechiae as part and parcel of the disease; this organism may be

cultivated from smears made from petechiae. Thus the presence of a petechial rash does not mean a poor prognosis just as the absence of a rash does not necessarily indicate a good outcome.

Hain (1951) stated that the range of circulating eosinophils for the child in apparent health was 109 to 359 per c.mm. The range in the initial counts for children experiencing acute febrile illnesses was 0 - 97 per c.mm.

Faloon et al (1950) quoted Thorn who suggested that the eosinophil count could be used in the diagnosis of the Waterhouse-Friderichsen syndrome and in its treatment. In the patients with generalised sepsis, adrenocortical function would be expected to increase and the eosinophil count would fall. In cases of Waterhouse-Friderichsen syndrome where overwhelming sepsis and adrenocortical failure were produced by haemorrhage into the adrenal glands, the eosinophil count would be expected to rise. The subsequent administration of adequate amounts of whole adrenocortical extract should then reduce the number of circulating eosinophils. Adequate replacement therapy could be controlled by repeated eosinophil counts.

Hodes et al. (1952) described their experience with eosinophil counts in meningococcal infection in

mild or moderate degree. Nine of his patients showed eosinophil counts of under 25 per c.mm., and 8 had a count of 0. In 3 cases, all critically ill and all clinically diagnosed Waterhouse-Friderichsen syndrome a total eosinophil count little if any below the normal level was found. They concluded that their findings lent support to the belief that adrenal cortical function may be impaired in patients with overwhelming meningococcal infection.

In the present series, in 13 moderately ill patients total eosinophil counts were done, when the count was zero. Eight of these patients had petechial rashes, and 4 were treated with steroids. None of the severely ill patients had total eosinophil counts carried out. All of the 13 patients survived. As Gardner (1956) suggested, it would be worthwhile to pay attention to peripheral circulation, blood pressure and total eosinophil count in the management of patients in whom circulatory failure and toxaemia might be thought to be impending.

Wasz-Hockert and Hjelt (1956) from their studies of adrenals removed from autopsies stated that in fatal cases of purulent meningitis the typical alarm reaction phase with increased cellular activity was found. This was followed later by exhaustive phase, and it seemed obvious that the adrenal cortex cannot keep up

the production demanded. They suggested adjuvant therapy using ACTH, cortisone and hydrocortisone.

Griffin and Daeschner (1954), in considering the pathogenesis of the Waterhouse Friderichsen syndrome, pointed out that adrenalectomised dogs survived for about 7 days without replacement therapy. Unlike the course following the removal of the adrenal glands in otherwise normal animals, it is evident in the Waterhouse-Friderichsen syndrome that the exhaustion of the adrenal cortex occurs incidentally to the stress imposed by severe infection.

Thomison and Shapiro (1957) wrote that in addition to patients showing the typical Waterhouse-Friderichsen syndrome, many patients died with purpura and vascular collapse due to meningococcal septicaemia, but at autopsy failed to show the anticipated adrenal lesions. Of 146 cases of proved meningococcal septicaemia, 30 typical cases of Waterhouse-Friderichsen syndrome recovered within 3 to 8 days. These cases were considered to have shown temporary adrenal insufficiency. Two fatal cases who showed massive adrenal haemorrhage were receiving cortisone plus chemotherapy and antibiotics. It was concluded that changes in the adrenal, other than massive haemorrhage, are reversible with complete replacement of destroyed tissue and restoration of function.

Death in face of adrenal replacement and anti-biotics emphasised the overwhelming nature of the disease and the absolute necessity for early diagnosis and institution of treatment of the infection itself.

Koch and Carson (1958) stated that prior to 1953 when adrenal steroids were not used, 7 patients with Waterhouse-Friderichsen syndrome were seen with 1 survivor. After 1953 there were 9 patients with 2 survivors. They commented that the fatality rate (from the Waterhouse-Friderichsen syndrome) had remained the same throughout the years, and that their data did not support the conclusion that hydrocortisone increased the chance for survival. They emphasised the necessity for early diagnosis and early treatment.

Alexander (1952) quoted D'Agati and Marangoni (1945) and stated that the adrenal injury in Waterhouse-Friderichsen syndrome was believed to be only a part of the fundamental lesion which appeared to be primarily damage to the endothelium of the capillaries, especially in the adrenals, liver, skin, kidney and heart. She thought that alteration by cortisone of the generalised abnormal capillary permeability might be the most important action in saving those patients who recovered.

May (1960) discussed circulatory failure (shock) in fulminant meningogoccal infection. He gave a

clinical description of classical (shock) circulatory failure to which was added purpuric lesions in the skin. Most often this was precipitated by infection with Gram-negative endotoxin-producing organisms of which the meningococcus was the most conspicuous offender in infants and children. Intravenous injection of minute amounts of meningococcal endotoxin into experimental animals produced manifestations of circulatory failure indistinguishable from these which occurred naturally in humans overwhelmed by meningococcal infection. He further stated that the primary lesion in overwhelming infection was a diffuse uneven damage and thrombosis in small vessels leading to variable degrees of haemorrhage in many organs - in the adrenals most conspicuously but not consistently or exclusively.

He further pointed out that animals who had adrenals removed abruptly and with care did not die in acute circulatory failure. The animals deteriorated slowly and the administration of a small amount of steroid afforded prompt relief. He contrasted the failure of steroid therapy to reduce the mortality from overwhelming (meningococcal) infection although deaths from meningococcal infection have fallen with the institution of therapy (e.g. after introduction of specific antiserum

mortality fell from 80% to 55%, and later with the addition of sulphonamides, to 10%). The death rate from overwhelming infection when meningococcal antiserum was the sole specific therapy was about 60%, with the addition of chemotherapy it remained at least 60%, and after the availability of steroids it was still 60% or higher.

The decision whether to use steroids or not might be helped by the absolute eosinophil count. Hodes et al. (1956) said, "the eosinophil count may be of aid in indicating whether injury to the adrenals of severe extent has occurred. When the adrenals are responding normally to infection, the eosinophil count is zero. When the adrenals have lost this ability to respond, counts about 50 - 75 c.mm. are found."

COMMENT:

In the series of 36 deaths, 3 patients were treated with Eucortone, and at post-mortem 1 showed adrenal haemorrhages, 1 showed absence of lipoid granules, and the other showed no suprarenal haemorrhage. Cortisone or similar substance was administered in 8 others, and post-mortem examinations were done in 6 of them. In one, bilateral supra-renal haemorrhages were found, in another some oedema but no haemorrhages, and in the remaining 4 there was no evidence of adrenal bleeding.

From this small series of deaths it is not possible to draw any firm conclusions as to the effect of steroid therapy. It is confirmed that the total circulating eosinophil count could be used in helping to differentiate those cases whose adrenal response is normal. This might be of aid in the treatment of patients showing circulatory collapse in fulminant meningococcal infection.

S E C T I O N II.

RESULTS.

There were 44 patients in this series of 251 who showed late manifestations of their illness, an incidence of 17.5%. Hutchison and Kovacs (1963) reviewed reported series and tabulated these - Table 15. This table is reproduced on page 50 , to which has been added the present series.

With the exception of Trolle's series, all the others were in the post-chemotherapeutic era, and overlapped the same period of time as the present series. It was calculated that 50% of the children were less than 1 year old at onset of illness, and that the "average mortality" was 14.4% and the "average sequelae rate" was 18%. The corresponding figures for the present series were: 43% of patients were less than 1 year old at onset of illness, the mortality rate was 12.5%, and 17% showed sequelae.

COMMENT:

These results show that although there has been a fall in mortality from the common forms of meningitis, there is still a large number of patients surviving with evidence of brain damage. Hutchison and Kovacs (1963) posed the question of whether the decrease in mortality meant the increased survival of children with varying degrees of cerebral sequelae. Earlier, in

1950, Davies, Meyer and Hyde had pointed out that more damaged children were surviving than previously because of better treatment and that the problem of these children was one of increasing magnitude as treatment improved.

TABLE 15

Summary of Review of Literature (after Hutchison and Kovacs)

Author	Year of Study	Number of Cases	Type of Meningitis	Mortality Rate	Cases at Follow-up	Sequelae
Trolle	1920-1945	525 mostly children	Meningo-coccal	Pre-Chemo 65.8% Post do. 11.9%	313	Pre-chemo. 54% (41% severe Post-Chemo. 50% (17% severe)
Crook et al.	1941-1948	110 (52% less 1 yr. old)	Influenzal	21%	64	17% of whole series
Alexander	1954	189	Purulent*	13.0%	-	12% (of survivors)
Desmit	1949-1954	114 (60% less (2 yr of age)	Purulent*	8.5%	102	14% (of total series
Bergstrand	1947-1954	92	Purulent*	7.6%	77	19% (of survivors)
Smith	1944-1953	409 (47% less 1 yr. old)	Purulent*	31.0%	-	18%
McNiel	1950-1957	117 (50% less 1 yr. old	Purulent*	1 5%	97	24% (of total)
Hutchison	1952-1956	122 (55% less 1 yr.)	Purulent*	9.8%	41	26%
Present Series	1946-1951	287 (43% less 1 yr old	Purulent*	12.5%	251	17.5%
Average		50% less than 1 yr. old	Purulent*	14.4%		18%

*The term "purulent" is synonymous with "pyogenic".

RESULT OF FOLLOW-UP OF PATIENTS.

METHOD EMPLOYED:

Where the patient was of school age the Head Teacher was contacted and invited to give a short account of scholastic ability. Specific questions were asked:

(a) is patient in a class for his age and is he maintaining his place?

(b) if at school before illness, has there been deterioration since illness?

(c) has there been any change in behaviour?

(d) any other observations.

In the child of pre-school age the majority were seen personally, but where not a proforma was sent to the Family Doctor asking about the child's mental status and asking specific questions such as:

(a) has the child had convulsions since illness?

(b) is there any evidence of spasticity, blindness of deafness?

(c) is hydrocephalus present?

(d) any other observations.

Where any report suggested doubtful impairment of intellect or other sequelae, a second report was requested after an interval of 2 years.

There are limitations to this method of

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assessment. First is that a child doing poorly at school might have had a lower intellect anyway and his illness had had nothing to do with it. The point is suggested in some of the case reports which follow. Second is the fact that this study is retrospective. Some of the children who were admitted in 1946 had left school several years before reports on them were requested, and the teacher most involved was no longer on the staff of that school. Third, because of the movement of families, environmental factors have been difficult to assess. However, here again some of the case reports comment on this point.

Lastly the assessment has not been done solely by one person as school masters and Family Doctors have given their opinions.

Nevertheless, even with these limitations, analyses of the reports show convincing evidence of brain damage and neurological involvement which can be attributed to the patient's meningitis.

There were 6 of the 26 patients with pneumococcal meningitis who were considered to show late manifestations of their illness - an incidence of 23%.

Results:

These findings are recorded in Table 16:

TABLE 16

LATE MANIFESTATIONS IN PATIENTS WITH PNEUMOCOCCAL MENINGITIS

CASE	Age on Admission	Time till Temp. normal	Streptomycin	Convulsion/ Coma on Admission	Skull Fracture	Subdural Effusion	Disability
Sylvia W	1 yr 10mth	21 days	-				Deafness but normal intelligence
Leonard M.	1 year	36 hours	-	Coma	-	-	Lacking in concentration and impaired intellect.
George W	11 years	12 days	Yes	Coma	yes, 1yr prev.	Burr-holes, no effusion	Impaired intellect.
Peter C.	6½ yrs	36 hours	-	Coma	-	-	Deafness but normal intelligence.
John M.	7½ yrs	48 hours	-	-	yes. 7 weeks prev.	-	Behaviour problem with impaired intellect.
Sheenagh T	5 weeks	6 days	-	-	-	Bilat. Effus.	Weakness of right hand - slow to attain milestones.

Deafness with normal intelligence	2	Total 6
Impaired intellect	1	
Impaired intellect with lacking in concentration	1	
Impaired intellect with behaviour problem	1	
Weakness of R. hand - slow to attain milestones.	1	

RESULT OF FOLLOW-UP OF PATIENTS WITH PNEUMOCOCCAL MENINGITIS.

There were 4 males and 2 females in the group with ages varying from 5 weeks of age to 11 years.

The time taken for the temperature to fall to normal was prolonged in 3. Ingraham and Matson (1954) have suggested that certain focal neurological signs such as inequality of pupils, vomiting, bulging fontanelle may be suggestive of subdural collections in infants and in older children, one other sign is the temperature remaining elevated for more than 48 - 72 hours despite adequate therapy. In the 3 patients whose temperature took longer than 72 hours, burr holes were done in 1, the boy aged 11 years, and no collections were found in the subdural spaces. In a second, the baby aged 5 weeks had subdural taps carried out and fluid was found on both sides. This was treated by daily tapping - no craniotomy was carried out. In the third case, the girl aged 1 year and 10 months no investigations were carried out. It is not possible to make any comment in this case. Thus in the 3 patients whose temperature remained elevated 2 of the 3 were investigated and subdural effusion was found in one.

In one patient only was streptomycin administered and no signs of deafness were found.

Three of the 6 were admitted in coma. Two of the children have a history of skull fracture - one had occurred 1 year previously; the other 7 weeks beforehand. Galloway and Chambers (1953) reported on skull defects and fractures in relationship to pneumococcal meningitis. They pointed out that remote fractures as well as recent fractures could have been the cause of the meningitis. In the 2 patients mentioned above the fracture line went through a frontal sinus, and it was considered this was the route entry of infection. Both of them showed impairment of intellect and one in addition had a behaviour problem. There were two other children with skull fractures in the pneumococcal group. Neither of these two patients showed sequelae. The trauma causing the fracture of the skull in these who developed sequelae might also have caused brain damage which became apparent only after the meningitis. However, there was no history of any change in these children following their skull fractures. As to the disabilities 2 had normal intelligence but were deaf. In the case of Sylvia W. the family Doctor reported "this family are now in Kenya, and Sylvia is a pupil of Kenya High School, Nairobi. I believe that Sylvia's health is very good except for some deafness".

The other patient, Peter C, attends a School for the Deaf. His head teacher wrote "although he has complete nerve deafness the boy is a most promising pupil with well above average abilities. In the words of his teacher "he is a joy to teach. He is remarkably well adjusted with a pleasant and friendly nature." Report from E.N.T. Consultant "this boy, as you say, is stone deaf after his meningitis and there is no cochleo-palpebral reflex. Examination shows nothing abnormal in the ears, nose or throat. Special schooling will accordingly have to be arranged."

Leonard M. had impaired intellect and lacked concentration as will be seen from his report "I.Q. 83 on Terrman Merrill Test done by the Educational Psychologist. His progress has been correspondingly slow. At one stage he seemed to have an abnormal lack of concentration, even for listening to a story, but this is no longer apparent. Up to the age of 9 he was abnormally timid. Reading age 8 - 9 years. Leonard is a normal backward child of low intelligence". His actual age at this time was 10 years 8 months. A further report was requested 2 years later and was as follows "His progress is very slight, he finished 25th in 25 pupils in our lowest stream. There seems nothing abnormal about him, he works as well as he is

able to, though that standard is low. We have no indication of deafness. There seems to be no behaviour problem."

John M. had impaired intellect and a behaviour problem. His teacher's report was "very slow and retarded in all subjects. His general behaviour and industry appear to have deteriorated since his illness."

George W. showed impaired intellect as will be seen from his school report "This boy is now fishing from Macduff. He left school on 15.9.50., returned on 3.1.51., and finally left from a modified class on 24.8.54. I have not seen him since he left school. His intellect was then impaired."

In the case of the last patient, Sheenagh T., she had definite weakness of the right hand which when last seen was slowly improving. Her mental milestones were slow.

SUMMARY:

Of the 6 patients showing late manifestations of pneumococcal meningitis 3 were comatose on admission. Two had had fractured skulls and 1 proved subdural effusions. In 1 case only had streptomycin been administered.

RESULT OF FOLLOW-UP OF PATIENTS WITH UNIDENTIFIED TYPE MENINGITIS.

METHOD EMPLOYED:

The same method of follow-up was used as in the other forms of meningitis.

There were 18 of the 79 patients with unidentified type meningitis who were considered to show late manifestations of their illness - an incidence of 22%

RESULTS:

The principal results are given in the following Table (Table 17.)

TABLE 17

LATE MANIFESTATIONS IN PATIENTS WITH PURULENT MENINGITIS

Case	Age on Admission	Time till Temperature normal	Streptomycin	Convulsions or Coma on Admission	Disability
Alistair S.	5 yrs	4 days	-	-	Behaviour problem:impaired intellect.
Alistair McA	9 1/12 yr	3 days	-	-	Behaviour problem: impaired intellect.
Mary B.	4 yrs	9 days	-	-	Lacks concentration:normal intellect.
William S	8 yrs	4 days	-	Convulsions	Lacks concentration:normal intellect.
Gordon A.	8 yrs	2 days	-	-	Lacks concentration:normal intellect.
Robert B.	1 7/12 yr	2 days	-	-	Lacks concentration:normal intellect.
Stanley C.	10 yrs		-	-	Impaired intellect.
Charles D.	1 yr	12 days	-	-	Deaf: Behaviour problem.
Agnes F.	3 mths	3 days	-	Convulsions	Impaired intellect.
Sandra A	9 mths	3 days	-	Convulsions	Deaf: normal intellect.
George W.	13 mths	4 days	-	-	Impaired intellect.
Ian J.	2yr 1mth	2 days	-	-	Impaired intellect.
Muriel R.	3 mths	3 days	-	-	Impaired intellect.
Colin F.	2 yrs	2 days	-	-	Impaired intellect.
George K.	3½ yrs	2 days	-	Coma	Impaired intellect.
Hugh D.	5 yrs	afebrile	-	-	Impaired intellect.
Patricia B.	5 yrs	afebrile	-	-	Impaired intellect.
Ian McL	8 yrs	36 hours	-	Coma	Behaviour problem.

Behaviour Problem with impaired intellect	..	2	Total 18
Lacks concentration with normal intellect	..	4	
Impaired intellect	..	8	
Impaired intellect - lacks coordination	..	1	
Behaviour problem with deafness	..	1	
Deafness with normal intellect	..	1	
Behaviour problem	..	1 ?	

In this group there were 13 males and 5 females. There were 4 under the age of 1 year, 8 between the ages of 2 years and 5 years, and 6 between the ages of 6 and 10 years.

The temperature remained elevated for more than 72 hours in 5 patients. In another 2 the patient was afebrile throughout.

Three patients had convulsions on admission and 2 were comatose. The duration of symptoms prior to admission was 72 hours or less in 13 patients, and over 72 hours in 5.

The length of stay in hospital was less than 3 weeks in 14 and over 3 weeks in 4.

None of the patients in this group was treated with streptomycin.

INDIVIDUAL REPORTS:

Alistair S. The headmaster reported "I find Alistair to be very indifferent both towards his work in school and also in his attitude to his class-mates. He reads fluently but without comprehension. Although his number work is accurate, it is very slow and he is very slow to grasp anything new, in this subject. His written work is neat and tidy."

Alistair McA. The report on this boy was "Progress at school still satisfactory, but average ability slightly retarded. Behaviour - not quite so lively; inclined to be a little sullen when checked; - a factor quite unknown before illness."

Mary B. The teacher stated here "Mary's progress is very slow, but she is a very nice little girl to work with - has developed quite an amount of concentration and tries very hard. The brother who has not suffered from meningitis is much slower than Mary, and her whole background is rather poor. Mary cannot keep pace with the average group but is progressing alowly."

William S. The report on this boy was "This pupil was far behind the class when he returned to school (after his illness). He found it very difficult to sit still and to concentrate although he often does not hear when apoken to. He is careful but rather a slow worker."

Gordon A. His head teacher wrote "This boy is, at present, repeating a term in a second stream class. His behaviour and attitude in class are excellent but academically his work is very poor. Gordon lacks concentration and finds difficulty in following a task through to

the end by himself."

A further follow-up report was obtained $2\frac{1}{2}$ years later and was as follows "The above named lad left school when he attained leaving age. He left without having completed a three year secondary course as it was necessary on two separate occasions to ask him to repeat a term in a second stream class. This didn't in any way discourage him. He never ceased to try. He appeared to be genuinely interested in himself, and anxious, probably over anxious, to please his subject teachers. All his work was done to the best of his very limited ability although his handwriting left much to be desired (It is only fair to say, however, that his untidy practical work was believed to be due to over-anxiety or poor co-ordination or possibly both). Gordon was always honest and reliable. His attitude to School and his reactions to School discipline were often favourably commented on by members of the staff.

He kept himself clean and tidy, was, in fact, rather proud of his personal appearance.

His medical card indicated that his hearing was normal."

Robert B. The initial follow-up on this patient was "Robert, meantime in Class 4 B., is making quite good progress, but he is not yet by any means a fluent reader. He had an I.Q. of 95 at 7 plus level but works more intelligently than might be expected from this finding. In an average class of 20 he stands 12th. Inability to concentrate prevents quicker progress, and his teacher states that he seemingly can't sit still for any length of time. He does not resent correction or chiding but it makes little difference and he remains a restless lad."

A further report 8 months later stated "Robert can work well when he concentrates but this he seldom does. His reading, spelling and sums are well up to the average of the class though his written work is often "slapdash" and untidy. He is restless and unsettled when anyone is sitting near him. There is no sign of deafness in class. No change in behaviour has been noted. Robert seems quite happy in school both in classroom and in playground."

Stanley C. Was stated to be "simply at home, unable to do a normal job."

Charles D. The E.N.T. Consultant reported "My impression was that he is not entirely deaf as he seems to respond to low tones. He appears very intelligent and it may be necessary for him to go to a Special School for education in due course." Later the Head Master of a School for the Deaf wrote "was given to tantrums before admission. These have continued but there are signs of better adjustment socially. Appears to have quite good ability and is making satisfactory progress, except in speech, which presents him with very great difficulty."

Agnes F. This girl's school report showed that she was well below average and out of a class of 43 she was last but one.

Sandra A. Her teacher reported that Sandra had been absent so often that she had had little opportunity of showing much progress. She was not a clever child, but seemed happy in her work and tried hard. Her behaviour was good. She had had trouble with her ears and an operation for squint.

George W. This boy's progress at school was "very poor". Has been transferred to a second

stream class Vb_2 which is doing work usually finished in Primary IV. George was in Primary Va before being transferred to this newly formed class (Primary Vb_2). Does try to do well in school. Is well behaved."

A further report stated "Tries very hard in class - a Primary 6a class. George should be in 7a. Sat his transfer exam last November. Has been placed in a Modified Course. His 2 I.Q. marks in the examination were 87 and 76. No deafness."

Ian J. The first school report read "This pupil has a 9+ I.Q of 83. He is in a second stream class Primary Va_2 instead of being in a Primary VIb, his proper age group class. His place in class is low - 17th out of 20. Mechanical arithmetic is good for his mental ability. Problem arithmetic is poor. His English is fair for this class but would be poor in the class he should be in. He is in the lowest group for reading. Spelling is well prepared but he does not retain it for long. His behaviour is good."

A repeat report two years later stated "He is only in his first term here, but is well down near the bottom of a second stream class.

This conforms to his I.Qs in the Transfer Test. "Otherwise he is a bright enough child who prepares his work to the best of his ability, e.g. homework is always fairly well done but in school tests he is pretty poor."

Muriel R. The Rector of this girl's school gave the following facts "I am sorry to say that she continues to make poor progress. She has completed the Third Year of our Domestic Course without a language, her pereentage marks for the session being English 19, Geography 14, Mathematics 34, Science 22, Art 52, Homecraft 45. Her Form Teacher, who takes her for Homecraft, says that she is not a good worker. No evidence of deafness."

A further report was obtained 2 years later and stated "This girl followed the Domestic, non language course until she left school. She was having to repeat the Third Year, having done very poorly indeed in the first session in which she was placed in that Class."

Colin F. Of this boy the teacher wrote "Colin is keen and very hard working. Is in a 3rd stream class following a modified course. Although he reads extremely slowly he is painstaking and willingly tackles full length boys' novels. He

uses the school library at lunch time. In written work he is very slow to learn. In technical subjects he is handicapped by a lack of co-ordination. He willingly takes part in class activities and generally 'fits in'."

George K. Initial school report was "Lethargic appearance and slovenly manner. Dislikes strenuous games, work careless and untidy. Stayed extra term in hope of obtaining a certificate, but failed to do so. Had no aptitude for practical work. On occasions displayed a surprising amount of commonsense." His performance was rather below his mental ability, according to the results of his Transfer Test. His last year showed him 15th in 20 and 15th in 17, in a very ordinary second stream class. There was no indication of deafness. He presented no real problems of behaviour apart from his lethargic and slovenly approach to his work."

Hugh D. This lad's "Progress at school - very little. He was slow and most untidy in his work."

Patricia B. The headmaster stated "The I.Q. of this girl was 71. She was placed in an adjustment class and throughout her course was very "poor" pupil. She made very little progress. Only in arithmetic could she be adjudged average

in that class. In other subjects she was well below average."

Ian McL. This patient's school could not be traced. The family doctor obtained the following details "I have managed to get some information from his grandmother "Ian McL was an evacuee from London at the time of his meningitis. His grandmother considered him to be a fairly irresponsible and useless chap who has not settled in any job. He was a deserter from the Army."

RESULTS OF FOLLOW?UP OF PATIENTS WITH MENINGOCOCCAL MENINGITIS.

METHOD:

The same method of follow-up was used as in the other forms of meningitis.

There were 12 of the 116 patients with meningococcal meningitis who were considered to show late manifestations of their illness - an incidence of 10%.

RESULTS

The principal results are recorded in the following Table (Table 18.)

TABLE 18

LATE MANIFESTATIONS IN PATIENTS WITH MENINGOCOCCAL MENINGITIS

CASE	Age on Admission	Time till Temperature Normal	Streptomycin	Convulsions of Coma on Admission	Disability.
Leslie W	3 mths	14 days		Convulsions	Hydrocephalus:Ineducable
Robert M.	5 mths	24 hours	-	-	Deaf L.ear:normal intellect.
Alexander W.	5 mths	14 days	-	-	Behaviour problem: impaired intellect.
James R.	5 mths	7 days	-	Convulsions	Behaviour problem: normal intellect.
James P.	14 weeks	10 days	-	Convulsions	Behaviour problem:impaired intellect.
Raymond B.	8 mths	3 days	-	Convulsions	Lacks concentration:normal intellect.
Peter R.	6½ yrs	36 hours	-	-	Lacks concentration:impaired intellect.
William S.	7 months	4 days	-	-	Behaviour problem:impaired intellect.
Michael R.	4 yrs	3 days	-	-	Behaviour problem:impaired intellect.
Rory T.	5 months	?	-	-	Deaf:impaired intellect: Hydroceph.
Bernard D.	2½ yrs	24 hours	-	Coma	Lacks concentration:impaired intellect.
Charles M.	3 yrs	24 hours	-	-	Deaf: impaired intellect.

Behaviour Problem + impaired intellect - 4
Deaf: normal intellect .. .. - 1
Deaf: impaired intellect .. .. - 2
Behaviour problem + normal intellect - 1
Lacks concentration + impaired intellect - 2
Lacks concentration + normal intellect - 1
Hydrocephalus and ineducable - 1

Total 12

All the patients were male.

There were 8 patients under the age of 12 months and of these 6 were under the age of 6 months. There were 3 between the ages of 2 years and 5 years and 1 over the age of 6 years.

The temperature remained elevated beyond 72 hours in 5 patients: in 1 it was not possible to state the time as the child was treated before coming under our care. In the remaining 6 patients the time taken for the temperature to fall was less than 72 hours. Of the 5 who took longer than 72 hours the actual times were 14 days in 2, 10 days, 7 days, and 4 days respectively.

Convulsions were presenting symptoms in 4 and one was comatose on admission.

Ten of the patients had symptoms of less than 72 hours duration - in 5 it was 24 hours, in 2 it was 48 hours, and in the other 3 it was 72 hours. In one (for reasons given above) the duration of symptoms is not known. In the other patient the time was 4 days.

Of the 11 whose duration of stay in hospital could be ascertained 9 were in-patients for less than 21 days and 2 for over 21 days.

INDIVIDUAL REPORTS

Leslie W. The Rector of the local school wrote "This boy has never been a pupil at this school. His sister is in our First Infants Class but she does not appear to know about her brother, who, I think, is in a Home. From what I have heard of his condition, I don't think it likely he will ever be able to attend a normal school."

Robert M. The school teacher reported "This boy was enrolled here in August, 1955 and has not had any severe illness since entering school. He appears to be deaf completely in the left ear, and strikes one as being a child who lives more or less in a world of his own.

Considering his handicap his progres has been fairly satisfactory although his innate ability is not on a high scale. His I.Q is 97. He has never been retarded but he requires extra attention to maintain the standard of the class. In the Infant and Junior Divisions he used to do quite a bit of lip reading."

E.N.T. Consultant report was "I have examined this boy. He has a nerve deafness in the right ear averaging a hearing loss of 30 decibels in the speech range. There is a mixed deafness in the left ear averaging a loss of 70 decibels. The latter, I think can be improved by politizerisation."

Alexander W. Attends a Special School and his progress was reported "Alex has made some progress in reading which is now a little more accurate, and when he can be encouraged to settle down to number work he does manage simple addition without concretes.

Reading age	5 years 6 months
Addition	6 years 3 months
Subtraction	5 years 9 months

Spelling and Writing are very poor.

Actual age at this time was 8 years 6 months.

Behaviour is childish and immature even for his mental age. Alex is inclined to be greedy and sulky. Alex is the fourth member of a family of five children, of whom 3 are mentally retarded and attend Beechwood Special School. Both parents were of low intelligence, and the mother, who is now deceased, was herself educated at Rubislaw Special School."

James R. The teacher wrote "Ability - a little below average for his age group. In attainments he works up to his mental age except in reading. In oral work he seems keen and interested and answers well. His work in English suffers because of his poor reading. He is given to periods of day-dreaming. Very often he is badly behaved.

Praise and encouragement bring only a temporary improvement. He frequently becomes a disturbing element in the class."

James P. School report "James is very immature and has made little or no progress in the school work. He cannot read at all - he counts, adds and subtracts up to 10 only with the help of concrete aid e.g. bricks. He counts in sequence up to 11. He is in the class with his contemporaries and plays quite happily with them but his attitude is often aggressive and he is usually in the centre of trouble. He will apply himself quite diligently to anything of a copying nature - hand control quite good."

Raymond B. Of Raymond's progress his teacher had this to say "Till recently this boy's progress has been below average. His attendance has been most irregular and his teacher is emphatic that this irregularity is due as much to an unsatisfactory home background as anything else. The mother pleads colds, lack of footwear, slept in, and a variety of other excuses, but the teacher is convinced a lot can be laid down to some form or other of parental neglect. Last year he was often out when he was supposed to be ill. He is still backward in reading but is beginning to understand and his number work is slightly below average. While proving

no trouble in class apart from irregularity in attendance, the teacher considers he is not a very reliable boy."

A further report 2 years later: "It is impossible to judge Raymond's progress at school as his home conditions have, if anything, deteriorated since the last report. His mother has been in and out of hospital and seems to be incapable of running a home; his father is disinterested in his family; the whole family had to be cared for in the Children's Shelter for 4 months. Obviously, therefore, there is no hope of assessing Raymond's real progress. His actual progress is very unsatisfactory, he is inattentive, lacks concentration, is an unwilling attender, but all this is due to the home background, not tto any real retardation or backwardness. I would assess him as slightly below average pupil under normal circumstances, a boy who could do average work and in all respects be an average boy. There is no trace of any pre-school medical circumstances influencing his progress in any way and no trace of deafness.

Given the chance he could be quite a decent child. His present home circumstances will never give him that."

Peter R. School report showed "very little evidence of progress at school. He is in a modified class and is not doing well even in this lowest stream of the school. He is restless and his span of concentration is very short. Comparing achievement in primary and in secondary my impression is that he has not deteriorated: he was always a backward pupil even in the infant class."

William S. The teacher reported "Progress unsatisfactory - difficult child."

The Children's Officer under whose care this patient is wrote "This child, who, on discharge from the City Hospital was placed in Arnha Baby Home, is now boarded out with foster parents who are apparently getting on quite well with him, and we have no complaints of his behaviour from them."

Michael R. School teacher's report "Progress - very backward. In a section of PIII doing a very modified course. No interest in school work. Unsettled - tends to misbehave."

Rory T. The family doctor's opinion - "Is a bright lively boy. Seems a normal child mentally apart from retardation due to total deafness. Does not walk alone but takes a few steps by himself occasionally."

Bernard D. School teacher reported: "Bernard's progress remains the same. He is in lowest group of class and though he tries hard his work is erratic. He cannot concentrate for very long - is easily distracted. He is always very restless even when occupied with given consignments grouped according to his ability."

Charles M. Attended a school for the deaf when his teacher reported "very slow. Admitted to this school in 1950 and from records he was an extremely bad behaviour problem. Now he is a very good natured child and behaves very well and is willing worker making slow progress. He is still very backward".

The E.N.T. Consultant reported "I regret to say that following his meningitis he has no response to the loudest stimulation and has a complete bilateral nerve deafness. He should, of course, receive special schooling and I am communicating with the School Medical Officer concerning this. I do not expect any action will be taken until he has reached school age. His deafness is so great that a hearing aid will be of little or no value."

A further report two years later from his teacher stated "since the original report Charles has had two outbursts of really violent temper which occurred within weeks of each other at the beginning

of this year. He was treated by his own doctor immediately. Apart from these two lapses he is well behaved and good natured. Recently he has shown slight improvement educationally but he is still very backward. He has, however, shown a marked improvement socially. We hope this will continue. He has been in a class of boys of his own age for about nine months. Apart from certain subjects special arrangements are made within the class to cater for his backwardness. He has only three islands of hearing at 125 c.p.s, 250 c.p.s., and 400 c.p.s. ranging from 55 decibels to 80 decibels to 105 decibels.

On all other frequencies he shows no response to sound."

RESULTS OF FOLLOW-UP OF PATIENTS WITH INFLUENZAL MENINGITIS.

METHOD

A similar follow-up was employed in this type of Meningitis.

There were 7 of the 21 patients with Influenzal Meningitis who were considered to show late manifestations of their illness - an incidence of 33%.

RESULTS

The principle results are tabulated in Table 19.

TABLE 19

LATE MANIFESTATIONS IN PATIENTS WITH INFLUENZAL MENINGITIS

CASE	Age on Admission.	Time till Temperature Normal	Streptomycin	Convulsion or Coma on Admission.	Disability
Ian M.	8 months	$8\frac{1}{2}$ weeks	-	Convulsions	Idiot: Epileptiform Seizures.
Wilma D.	9 months	14 days	Yes	-	Impaired intellect.
Alice F.	8 months	10 days	Yes	Convulsions	Certified mentally deficient and admitted under care.
Joan K.	10 months	90 hours	-	Convulsions	Normal intelligence: ? Petit Mal.
Graham McD.	9 months	never elev.	-	-	Mentally retarded: deaf.
Lynn W.	8 months	14 days	Yes	-	Normal intellect: Left hemiplegia.
Richard W.	15 months	10 days	-	-	Impaired intellect: Petit Mal.

Deafness - mentally retarded	.. ..	- 1	
Idiot - grand mal epilepsy	.. ..	- 1	
Normal intellect - left hemiplegia	.. ..	- 1	
Normal intellect - petit mal	.. ..	- 1	Total
Impaired intellect + petit mal	.. ..	- 1	7
Certified mentally deficient	.. ..	- 1	
Impaired intellect	.. ..	- 1	

In this group there were 4 females and 3 males. Three patients were aged 8 months, 2 were 9 months and another was 10 months old, and the other was 1 year and 3 months.

It will be seen that in 6 of the 7 cases the temperature remained elevated for more than 72 hours. In fact in one case it was elevated for over 8 weeks. In one patient the temperature was never elevated.

Three of the patients had convulsions on admission. Ian M. had almost continuous convulsions on and off for a month. The other patients settled quickly on treatment.

The duration of symptoms prior to admission was prolonged beyond 72 hours except for one, the longest being 21 days.

The length of stay in hospital was 85 days, 20 days, 47 days, 17 days, 14 days, 39 days and 38 days respectively. Thus three remained in hospital for less than three weeks; the other three for much longer. This could indicate a more severe illness.

Three of the patients were treated with streptomycin. None of them became deaf.

INDIVIDUAL REPORTS:

Ian M. The family doctor reported " This child is an idiot. He has never learned to do anything for himself and in my opinion is quite incapable of learning. He cannot speak, uttering only animal noises. He continues to have epileptiform seizures."

Wilma D. This girl's teacher reported "Stage reached Primary VI; she was not fit for Primary VII. She is good at reading; her composition work is average; she is slow at mental arithmetic. Written work in arithmetic is average. She tries hard."

Alice F. This girl was certified and admitted to a Home. This child was considered to be ineducable.

Joan K. At follow-up at age of 4 years she was considered to be very well mentally and physically. She gave a history of petit mal like attacks. Investigations including E.E.G. were negative.

Graeme McD. This boy's family doctor wrote "Might be some mental retardation. Is three years old and can only say "Mum". Seen at E.N.T. out-patients at age of 3 years and fitted with a

transistor aid on account of deafness. Loss of hearing appears to be fairly evenly distributed throughout the speech frequency."

Lynn W. This child was seen many times at follow-up clinic and initially she was considered to be mentally retarded. She was illegitimate and her home circumstances were very poor. When last seen at the age of 3 years there was a dramatic change in her mentality. She still had her hemiplegia but was considered to be normal mentally. The change in her was coincidental with her being taken over by a foster mother.

Richard W. The Senior Assistant Medical Officer (Schools) reported, "Richard was not placed on the "handicapped list" as a pre-school child, but since entering school his progress has been slow and there has been concern about his apparent lack of co-ordination and concentration. He had already been referred to the Educational Psychologist who finds his I.Q. to be 77. He was investigated in the Children's Hospital following one or two "Petit mal" attacks. Although the E.E.G. is reported to have shown irregularities at that time, the child does not seem to have been on any therapy and meantime there have been no further symptoms of that kind.

There is no history of developmental delay or family association with the Special School and his vision and hearing are normal. Time may be all that is necessary in the ordinary school for him to catch up. He was re-tested again a year later. The psychologist wrote, "He was rather shy and inhibited in answering questions and there is the possibility that his slight negativism resulted in a failure to do justice to his abilities on the tests. I am not entirely convinced that this was the case, however, as he did co-operate quite readily on the easier items, and generally showed very slow and dull cerebration and perseveration in his responses. He was, moreover, industrious on the tests in a quiet way.

I regret to report that his current performance on the Stanford Binet Intelligence Scale, Form L-M, is well below the level which you quote from his school assessment, and at the present interview he obtained a mental age of 4 years 8 months, I.Q. 54. The scatter of his successes ranged from the $3\frac{1}{2}$ to 5 year level (actual age 8 years) and he did particularly poorly on items involving memory."

It will be seen then that of this group 2 were considered to have normal intelligence but had other neurological residua viz., petit mal and left hemiplegia. Five showed severe mental retardation and in addition 1 was deaf and 2 others had epileptiform seizures.

Analyses of results of the 44 patients found to have sequelae.

A brief report on each of the 44 patients has been given. It was decided to analyse these reports and it was found that the majority fell into four main groups. These results are given in Table 20.

It will be seen that impairment of intellect accounted for the highest number of those who developed sequelae and totalled 12. There were 9 with behaviour problems and of these, 7 had impaired intellect. Deafness accounted for 8, one of them had a behaviour problem in addition, 3 had impaired intellect and 4 had normal intellect (Nerve deafness was confirmed by audiometry in 5 of these patients; none had had streptomycin therapy). Of the remaining 6 patients, 1 had hydrocephalus and was ineducable; 1 had monoplegia and was slow in attaining mental milestones; 1 was suffering from grand mal and was considered to be an idiot; 2 others were of normal intellect but 1 had hemiplegia and the other had petit mal; the last was certified mentally defective.

It will be seen that the majority of these patients had more than one symptom. Trolle (1951) thought the mental symptoms were hardly ever single,

TABLE 20.

ANALYSES OF 44 PATIENTS SHOWING SEQUELAE.

Sequelae		Meningo.	Unidentified	Influenzal	Pneumoc.	Mixed	Coliform	Convulsions and or/coma	Total	
Impaired Intellect		-	8 coma convul	2	1 coma	-	1 convul	2 convul 2 coma	12	
Behaviour Problem	Normal Intellect	1 conv.	1 coma	-	-	-	-	-	2	9
	Impaired Intellect	4 conv.	2		1	-	-	2 convul 1 coma	7	
Deaf	Behaviour Problem	-	1	-	-	-	-		1	8
	Normal Intellect	1	1 convul	-	2 coma	-	-	1 convul 1 coma	4	
	Impaired Intellect	2	-	1	-	-	-	-	3	
Lacks Concentration	Normal Intellect	1 conv.	4 convul	-	-	-	-	2 convul	5	9
	Impaired Intellect	2 coma	1	-	1 coma	-	-	2 coma	4	
Hydroceph Ineducable		1 conv	-	-	-	-	-	1 convul	1	
Normal Intellect	Hemiplegia	-	-	1	-	-	-	-	1	2
	Petit mal	-	-	1 Conv	-	-	-	1 convul	1	
Certified M.D.		-	-	1 convul	-	-	-	1 convul	1	
Milestones slow & Hemiplegia		-	-	-	1	-	-	-	1	
Idiot & Grand Mal		-	-	1	-	-	-	-	1	
Total		12 (4 convul 1 coma)	18 (3 conv 2 coma)	7 (2 conv)	6 (3 coma)	-	1 (1 conv.)	10 convul 6 coma	44	

and among the recognised symptoms were emotional instability, impaired memory, undue restlessness and inability to concentrate. Defects of intellect were rarely found in his experience. He quoted Voison and Paisseau (1910) who found that 6 of 10 children discharged after cerebrospinal meningitis as normal had sequelae when followed up. These were children who had been previously gentle and had become difficult with violent choleric crises, pronounced emotional instability, irritability and restlessness.

Bradley (1957) wrote that "though not all children who survive illness or injury which might produce cerebral trauma are actually subsequently handicapped by sequelae of such experiences, a significant number come to later clinical attention." He went on to describe a series of individual symptoms strongly suggestive of brain injury. The most important of these were:-

(a) Unpredictable variability in behaviour. The parent may say the patient has good days and bad days, and the teacher may report excellent retention of school material at one time and apparent lack of familiarity with it at other times. In contrast to most children, whose variations can be accounted for by preceding events which have recently occurred, the brain-injured child shows no logical pattern.

(b) Hyperactivity. This may also be described as hyperkinesis, restlessness or agitation. The child who "constantly wanders about the classroom."

(c) Distractibility. This is probably synonomous with "Short attention span", and is particularly noticeable in the classroom. The teacher frequently states that "he would do well in school if he would pay attention long enough."

(d) Impulsiveness. This refers to the characteristic of the child who "acts first and thinks afterwards."

(e) Irritability. Irritability suggests ready excitability noted particularly when frustrating situations are encountered. They react to relatively minor irritations as though they were of immense and devastating importance.

(f) Difficulties in abstract thinking. Such difficulties are probably most obvious in children of school age and in the school situation. Arithmetic is commonly the subject which is most difficult. Even in younger children, poor concepts of number and quantitative values may be apparent.

It will be seen that in the case reports many of these symptoms are present.

Trolle (1951) obtained information from form-masters re psyche and school standards when it was found that about one-third of them were among the best in their class, one-third were medium and one-third belonged to the least intelligent of their classes. He concluded that impairment of intellect was not generally included among the mental disturbances following

meningitis. Silver (1958) described the behavioural syndrome associated with brain damage in children. He stated that the behaviour of a child with brain damage was not due to the brain damage alone, but was determined by the complex interrelationship of the child's biologic abilities and disabilities, his psychologic conflicts and defences and the environmental forces acting upon him. Hutchison and Kovacs (1963) stated that the significance of the various types of behaviour disorder and environmental defects could not be assessed. In 50% of those children identified as emotionally unstable, there was a history of behaviour disorder and "environmental defect" in the family.

COMMENT:

It would appear that many of the late symptoms following meningitis are those of brain damage. As reported by the above quoted authors, it is not possible to rule out environmental and hereditary factors.

Mechanism of brain damage

Trolle (1951) stated that the site of brain damage in patients with post-meningitis mental disturbances cannot be established, but there

could be no doubt that the process often extends beyond the meninges.

Desmit (1955) thought that meningo-encephalitis was a feature of the illness of 6 of the 15 patients who developed sequelae. In those who showed focal symptoms, no evidence of abscess or accumulation of subdural fluid was found.

Following the report by McKay, Ingraham and Matson in 1950 of collections of sterile fluid in the subdural space complicating influenzal meningitis, many similar findings were reported (Jones, 1952; Gulhkelch, 1953; Smith, 1954). Many theories as to the mechanism of production of these subdural collections were postulated (Spitz, Pollack and Angrist, 1945; Smith 1956; Arnold, 1951 and 1952). One of the generally accepted causes is that of haemorrhage from a cortical vein, probably one crossing the subdural space to reach a major venous sinus. The haemorrhage clots, the clot liquefies and eventually is surrounded by a semi-permeable membrane of fibrous tissue. The liquefied clot has a high protein content and can attract fluid by osmosis. In purulent meningitis such haemorrhage might arise from necrosis of the wall

of a vein involved in a process of thrombophlebitis.

Other authors had different theories. Smith (1954) thought that subdural effusions could follow subdural taps, and in several of the cases he reported it was not until the second tap that fluid was found. Williams and Stevens (1957) suggested that excessive withdrawal of cerebrospinal fluid for diagnosis might cause sagging of brain and tearing of cortical veins with subsequent effusion. Kneebone (1961) suggested that multiple drug therapy disallowed full action of the specific drugs used, or caused some specific effect by its very nature, which induced complications and sequelae.

Platou, Rinker and Derrick (1959) stated that the presence of subdural collections might reflect accompanying neurological damage rather than being the cause. The same authors pointed out that subdural collections were apt to occur in these youngest patients during the phase of rapid head growth. They suggested that diagnostic subdural taps be carried out in those patients whose response to therapy was atypical or unfavourable, and also added

convulsions, focal neurological signs, persistent fever, bulging fontanelle, rapidly increasing head size, projectile vomiting and opisthotonus. In the present series subdural collections were found in 2 patients. One of these was treated by craniotomy and made a full recovery. The other was treated by repeated subdural taps and was left with a monoplegia and retardation of mental milestones. Such collections were suspected in other patients but subdural taps did not confirm any such collection.

Smith and Landing (1960) said that severe brain damage might occur early in the course of influenzal meningitis in the absence of subdural effusions as well as in association with them.

Alexander (1952) considered that there was reason to believe that the (subdural) collection formed in response to damage to cerebral cells. She advanced the hypothesis that it was the resultant injury to cerebral cells which was responsible for abnormalities in the future mental development of patients with subdural collections rather than the effusion or the constricting effect of the membrane. It was well known that some infants exhibiting widespread cerebral damage early in the course of their

infection showed no subdural fluid, yet remained defective children.

Rorke and Pitts (1963) said that since subdural effusions are more apt to follow severe attacks of meningitis, satisfactory removal of membranes may not necessarily repair underlying brain damage and complete recovery may not ensue.

In 1942, Banks and MacCartney described 10 cases of meningococcal encephalitis, often fulminating. Galloway (1962) suggested it would seem reasonable to suppose that milder forms of encephalitis compatible with recovery could exist, and that some patients with sequelae might have had encephalitis as well as meningitis.

COMMENT:

From what has been said, several theories have been put forward to explain brain damage in the course of acute purulent meningitis. Several authors favour subdural collections, and others that the process extends beyond the meninges, involving the brain itself. It would seem that some of those developing sequelae either had a more severe illness or that they developed their illness at an early age when the brain was rapidly growing and consequently more vulnerable.

In the preceding section it has been suggested that those children who developed sequelae had a more severe illness. Trolle (1951) considered that the severity of the illness played a part in that there were, in his series, more showing mental disturbances in those who had been severely affected. Hutchison and Kovacs (1963) considered likewise that there was a positive correlation between the severity of the acute illness and the presence of neuropsychiatric sequelae.

Several workers have commented on the association of age at onset of the illness and the later development of sequelae. Davies, Meyer and Hyde (1950) found that the development of those children who were under the age of 2 years at the onset of their illnesses was in general considerably poorer than those 2 years of age or over. Trolle (1951) in his series investigated the age on admission and found that this was true where no chemotherapy was used. Bradley (1957) stated that clinical experience indicated that the majority of children with behaviour problems due to brain injury experienced their trauma early in life during the prenatal period, in association with the birth process, or during the first two or three years of infancy. The basic behaviour difficulties

of most of these children bore a striking resemblance to one another. Johnson (1960) in her series found that the greatest number of complications appeared in the youngest age groups. Hutchison and Kovacs (1963) concluded from their study that the mean age in years at the time of the meningitis was lower in the group who developed organic brain damage.

In the present series as a whole, 43% of the patients were under the age of 1 year. Of the 44 who developed sequelae, 20 were under 1 year, an incidence of 45%. It would appear, therefore, that almost half the patients who later developed sequelae were under the age of 1 year when they developed their illness.

COMMENT:

The results of the present section suggests that those patients who developed sequelae experienced their illness early in life and had had a severe illness.

S E C T I O N III.

TREATMENT.

Alexander (1952) wrote that minimal therapy was no longer justifiable and that with the availability of multiple effective agents optimal therapy must be the aim in all varieties of meningitis. She suggested the following guides:-

(1) A therapeutic programme which rapidly eliminated the meningeal infection.

(2) The use of at least two agents working through different modes of action.

(3) When possible the use of agents which in safe dosage, orally or parenterally, could maintain bactericidal concentrations in the cerebrospinal fluid without intrathecal injection.

(4) When there were other equally effective agents, avoid those which exhibited significant toxicity.

Desmitt (1955) in his series used penicillin intrathecally 10,000 units (repeated) and intramuscularly 20 - 50,000 x 3 hourly, and sulphadiazine 100 - 200 mgm. per Kg. body weight for all varieties except those due to haemophillus influenzae infection. For this type of meningitis he used the same drugs with streptomycin 40 mgm./Kg. in addition. Later, when available, chloromycetin 125 mgm./Kg. and sulphadiazine were employed.

Hodes et al (1956) suggested that influenzal meningitis should be treated with chloromycetin, sulphadiazine and penicillin; the last two drugs with other common varieties, using high dosage of penicillin in meningococcal infections.

Lepper and Spies (1957-58) had a similar programme, and in addition all received either ACTH or cortisone.

Platou et al. (1959) "flooded" patients with a combination of agents designed to combat the commonest causes of meningitis. The combination consisted of sulphadiazine 100 mg./Kg., chloramphenicol 100 mg./Kg. and penicillin 600,000 units. Dosage and interval of administration was varied according to conditions and continued for 8 days.

Kneebone (1961), pending bacteriological diagnosis, gave four drugs - penicillin, streptomycin, chloromycetin and sulphadiazine. After bacteriological confirmation, he treated the influenzal variety with sulphadiazine, chloromycetin with or without streptomycin, and meningococcal and pneumococcal with penicillin and sulphadiazine. Where the organism remained unknown, he continued to use all four drugs.

Jawetz et al. (1951) quoted by Alexander (1952), found no antagonism between penicillin and chloromycetin.

The following scheme of treatment was started in 1954 and was reported by Craig (1954).

1. All cases, pending bacteriological report on cerebrospinal fluid.

   (a) At the initial diagnostic lumbar puncture give 20,000 units of penicillin intrathecally. In addition, in the newborn, when the risk of coliform infection is high, give 25 mg. of streptomycin intrathecally.

   (b) Oral sulphadiazine, 120 mg. per lb (250 mg. per kg.) per 24 hours in infants (up to 1 year), 60 mg. per lb (120 mg. per kg.) per 24 hours in older children, divided into 4-hourly doses. The initial dose should be doubled.

   (c) Intramuscular penicillin, 1,000,000 units 2-hourly, 4-hourly or twice daily, according to the clinical severity of the illness. Two-hourly or 4-hourly dosage should be used in all cases in which meningococcal infection is thought unlikely.

2. When bacteriological diagnosis is established (normally within 24 hours)

(a) Meningococcal - No further intrathecal treatment. Continue sulphadiazine as above and penicillin 1,000,000 units twice daily, for at least seven days.

(b) Influenzal - No further intrathecal treatment. Continue sulphadiazine as above; discontinue penicillin. Give chloramphenicol 75 mg. per lb (160 mg. per kg.) per 24 hours, divided into four doses. Continue treatment for ten days.

(c) Streptococcal and pneumococcal - No further intrathecal treatment. Continue sulphadiazine as above. Continue penicillin 1,000,000 units 2-hourly, until C.S.F. is twice sterile, then 1,000,000 units twice daily. Continue treatment for ten days.

(d) Staphylococcal - Intrathecal penicillin 20,000 units daily, until C.S.F. is twice sterile. Continue penicillin 1,000,000 units 4-hourly. Discontinue sulphadiazine and give chloramphenicol, 75 mg. per lb (160 mg. per kg.) per 24 hours, divided into 4 doses. Continue for at least ten days.

(e) Coliform - No further intrathecal treatment. Discontinue penicillin. Continue sulphadiazine as above. Give streptomycin 20 mg. per lb (40 mg. per kg.) per 24 hours, divided into two doses. Give chloramphenicol, 75 mg. per lb (160 mg. per kg.) per 24 hours, divided into four doses. Discontinue streptomycin after 48 hours. Continue other drugs for ten days.

3. When the Waterhouse-Friderichsen syndrome is present

Give cortisone at once, 50 mg. intramuscularly and 50 mg. orally. After twelve hours give a further 50 mg. of cortisone orally or intramuscularly; then 25 mg. orally twice daily for a few days; then gradually lower the dose.

It has been very difficult to assess the effects of therapy as this study has been retrospective. However, it has been possible to divide the bulk of the cases of unidentified and meningococcal meningitis into three groups. A small number were treated with sulphonamide only, a larger number with sulphonamide mainly but also a small amount of penicillin up to a total of 10 mega (either intrathecally 20 - 40,000 units alone, or

intramuscularly less than 10 mega) The bulk were treated with large doses of penicillin 10 - 60 mega, and sulphadiazine or as stated in schedule above.

In an attempt to analyse the outcome in this series of patients various paths were explored. It has been stressed that the longer the symptoms before diagnosis and subsequent treatment, the worse the outcome (McKendrick,1954). Trolle (1951), however, pointed out that it could be that those cases who took longer to manifest their disease could be suffering from a less acute form. It was thought that this series could be examined to see if any conclusions could be reached as to the effect on late complications of such things as -

(1) duration of symptoms before hospitilisation;

(2) time for temperature to settle after institution of therapy - presuming that the speed with which temperature returns to normal is an indication of the efficacy of the treatment;

(3) duration of stay in hospital - the shorter the stay the better the response to therapy, bearing in mind that other conditions may prolong the stay, e.g. cross infection, intercurrent infection or other factors not

directly related to meningitis;

(4) whether any presenting symptoms, particularly convulsions and/or coma had an effect on prognosis;

(5) the distribution of the cell count in the cerebrospinal fluid;

(6) the age of the patient at time of admission;

(7) the type of organism causing the meningitis.

METHODS EMPLOYED:

The average duration of symptoms before hospitalisation, the average time for temperature to fall to normal and stay down and the average duration of stay in hospital were calculated for the group as a whole and the results for each group compared. Each group is comprised of "uncomplicated" and "complicated". The former means that the child has had no obvious late manifestations of the illness; the latter where the schoolteacher or other observer has given a poor report or where one or other of the late sequelae have been detected.

RESULTS

MENINGOCOCCAL MENINGITIS

TABLE 21

UNCOMPLICATED.

Therapy	No. of Cases	Average duration of symptoms before Admission	Time till Temperature Normal.	Stay in Hospital No. of days.
Sulpha only	5	2.2 days	2.1 days	12.2 days
Sulpha and Penicillin	41	2.1 days	4.0 days	15.4 days
Sulpha and High Penicillin	58	2.3 days	4.3 days	16.9 days
Average for whole group	104	2.3 days	4.1 days	16.2 days

COMPLICATED

Therapy	No. of Cases	Average duration of symptoms before Admission	Time till Temperature Normal.	Stay in Hospital No. of days.
Sulpha only	5	-	-	-
Sulpha and Penicillin	5	2.4 days	7.6 days	29.0 days
Sulpha and High Penicillin	7	1.6 days	3.9 days	15.5 days
Average for whole group	12	2.0 fays	5.5 days	21.6 days

Average duration of symptoms prior to admission.

It would appear from these tables, although some of the figures are small, that the average duration of symptoms prior to admission was the same in the complicated and uncomplicated groups, viz., 2.0 days and 2.3 days respectively.

Comment:

It would seem that the duration of symptoms prior to admission does not play a part in those who developed late manifestations.

Time till temperature fell to normal.

Comparing the complicated and uncomplicated groups till the temperature fell to normal, it can be seen that the average time was longer in the complicated group, 5.5 days as against 4.1 days. Where sulphadiazine and a small dose of penicillin was administered, the temperature took an average of 7.6 days to settle in the complicated group as against 4.0 days in the uncomplicated group. The corresponding figures were 3.9 days and 4.0 days when high doses of penicillin and sulphadiazine were employed.

Stay in Hospital.

The stay in hospital was shorter in the uncomplicated group as a whole 16.2 days as against 21.6 days.

Conclusions:

If it is accepted that the more efficient the treatment the quicker the temperature will be controlled, then it would seem that both groups show little difference in their response to therapy. However, the fact that the temperature was elevated for a longer time in the complicated group may be suggestive.

UNIDENTIFIED MENINGITIS

TABLE 22

UNCOMPLICATED

Therapy	No. of Cases	Average duration of symptoms before admission	Time till Temperature Normal	Stay in Hospital No. of days
Sulpha only	6	2.2 days	1.7 days	10.6 days
Sulpha and Penicillin	22	1.7 days	3.0 days	13.8 days
Sulpha and High Penicillin	32	1.9 days	2.3 days	12.6 days
Mixed	1	3.0 days	14.0 days	175 days
Average for whole group	61	1.9 days	2.7 days	15.6 days

COMPLICATED

Therapy	No. of Cases	Average duration of symptoms before admission	Time till Temperature Normal	Stay in Hospital No. of days.
Sulpha only	4	3.2 days	4.1 days	15 days
Sulpha and Penicillin	7	2.5 days	4.6 days	15.5 days
Sulpha and High Penicillin	7	2.5 days	4.0 days	18.0 days
Average for whole group	18	2.7 days	4.3 days	16.7 days.

It can be seen in the unidentified group that in the uncomplicated and complicated groups the average duration of symptoms prior to admission was much the same in both, being 1.9 and 2.7 days respectively. The average stay in hospital for both groups was virtually the same, being 15.6 days and 16.7 days respectively. The principal difference was in the time taken for the temperature to fall to normal, being 2.7 days in the uncomplicated group and 4.3 days in the complicated group.

Conclusions:

In this type of meningitis it seems that the difference in the time taken for the temperature to fall to normal is significant.

PNEUMOCOCCAL MENINGITIS

TABLE 23

UNCOMPLICATED

Therapy	No. of Cases	Average duration of symptoms before admission.	Time till Temperature Normal	Stay in Hospital No. of days
Sulpha and Penicillin	6	2.5 days	4.3 days	23.6 days
Sulpha and High Penicillin	14	2.4 days	4.6 days	23.7 days
Average for whole group	20	2.4 days	4.5 days	23.7 days

COMPLICATED.

Therapy	No. of Cases	Average duration of symptoms before admission	Time till Temperature Normal	Stay in Hospital No. of days
Sulpha and Penicillin	3	1.5 days	8.0 days	26.3 days
Sulpha and High Penicillin	1	1.0 days	2.0 days	37.0 days
Penicillin Sulpha, Streptomycin	1	1.0 days	12.0 days	41.0 days
Penicillin Sulpha Chloromycetin Terramycin	1	1.0 days	6.0 days	52.0 days
Average for whole group	6	1.2 days	7.3 days	34.8 days

In the "pneumococcal" group it will be seen that the average duration of symptoms prior to admission was 2.4 days in the uncomplicated group and 1.2 days in the complicated group. The duration of stay in hospital was 23.7 days and 34.8 days respectively. The time taken for the temperature to return to normal was 4.5 days and 7.3 days respectively.

Conclusions:

In this group it would appear that the duration of symptoms could have no bearing on the outcome as it was less in the complicated group. The duration of stay was longer in the complicated group and there was in particular considerable increase in the time before the temperature became normal in this group.

Thus again the time taken for the temperature to fall to normal is significant.

INFLUENZAL MENINGITIS

TABLE 24

UNCOMPLICATED

Therapy	No. of Cases	Average duration of symptoms before admission	Time till Temperature Normal	Stay in Hospital No. of days
Sulpha and Penicillin	2	2.0 days	18.2 days	64.5 days
Sulpha, Penicillin & Streptomycin	2	3.0 days	1.7 days	27.0 days
Chloro-mycetin	1	14.0 days	1.5 days	15.0 days
Penicillin, Sulpha Chloromycetin	8	2.4 days	5.0 days	19.0 days
Aerosporin	1	1.0 days	-	74.0 days
Average for whole group	14	3.1 days	6.3 days	30.2 days

COMPLICATED

Therapy	No. of Cases	Average duration of symptoms before admission	Time till Temperature Normal	Stay in Hospital No. of days
Sulpha and Penicillin	1	4.0 days	59.0 days	85.0 days
Sulpha Penicillin & Streptomycin	2	3.0 days	12.0 days	33.5 days
Sulpha and Chloromycetin	1	4.0 days	4.0 days	17.0 days
Chloromycetin	1	9.0 days	-	14.0 days
Sulpha, Penic. Chloromycetin Streptomycin	1	21.0 days	14.0 days	39.0 days
Sulpha, Penic. Chloromycetin	1	21.0 days	10.0 days	38.0 days
Average for whole group	7	8.1 days	18.5 days	37.1 days

The figures for comparison in the "influenzal" group are even smaller than in the other types. It can be seen that in the uncomplicated group the average time in all columns was less than in the complicated group. The average duration of symptoms prior to admission was 3.1 days in the uncomplicated group and 8.1 days in the complicated. The time till the temperature fell to normal was lower in the uncomplicated group, 6.3 days as against 18.5 days for the complicated group.

The average stay in hospital was 30.2 days for the uncomplicated and 37.1 days for the complicated.

Conclusion:

It would be assumed that in influenzal meningitis the longer duration of symptoms prior to admission might play a part in the subsequent development of late manifestations. The marked difference in the time taken till temperature was normal perhaps reflects the efficacy of chloromycetin in the treatment of this type of meningitis. Ten of the 17 patients had chloromycetin either alone or in combination with penicillin and sulphonamide in the uncomplicated group. Three of the 6 compli cated cases had chloromycetin either alone or in combination with penicillin, sulphonamide and streptomycin. The

longest time was where the patients in both groups were treated with sulphonamide and penicillin, neither of which was effective against the causal organism.

The temperature fell to normal quicker and the stay in hospital was less in the uncomplicated group.

"Mixed" Type

There were 9 patients in this group, and of the 5 who recovered, 2 had meningococcal septicaemia, 2 had staphylococcal infection and 1 had streptococcal meningitis. This last patient had a congenital cardiac abnormality and the meningitis was probably secondary to sub-acute bacterial endocarditis.

The ages of these patients were 6 months, 10 months, 4 years, 5 years and 6 years respectively. One of the patients was admitted in coma.

The following table sets out the type of therapy given, the average duration of symptoms prior to admission, the time till the temperature became normal, and the duration of stay in hospital for each patient. (Table 25)

TABLE 25

MIXED GROUP MENINGITIS

Type of Infection	Therapy	No. of Cases	Average duration of symptoms before Adm.	Time till Temperature Normal	Stay in Hospital No. of days
Menin. Septic	High Penicillin	1	24 hrs	3 days	49 days
Menin. Septic.	High Penicillin + streptomycin	1	24 hrs	1 day	16 days
Staphylo=	Sulpha, Pen., Aureomycin	1	48 hrs	8 days	34 days
Staphylo=	Sulpha,High Penicillin	1	24 hrs	3 days	24 days
Strepto=	Sulpha.High Penicillin & Aureomycin	1	72 hrs	14 days	29 days

All the patients were admitted under 48 hours of onset except one who had subacute bacterial endocarditis.

The temperature fell to normal in under 3 days in 3 patients; in the fourth 8 days and in the fifth 14 days. This last was again the patient with the subacute bacterial endocarditis.

Four of the patients were in hospital for longer than 21 days, the fifth patient was in hospital for 16 days. All five patients survived.

The cell count was normal in the 2 patients with meningococcal septicaemia. No cell count was done in one patient with staphylococcal infection, and it was 10,000 in the other. The patient with streptococcal meningitis had a cell count of 4,100.

In the follow-up of these 5 patients no complication was detected. Four of the patients were in hospital for longer than 21 days; two of those had other conditions which prolonged their stay, namely, purpura necrotica in one, and sub-acute bacterial endocarditis in the other.

One only had symptoms of more than 72 hours prior to admission.

The temperature fell to normal in less than 72 hours in 3 patients.

Conclusion:

There are too few patients in this group to draw any firm conclusions.

Coliform Group

There were 12 patients, and of the 4 who recovered from their illness, 3 had no sequelae and 1 was left grossly mentally retarded and spastic. Details of these patients are given below.

TABLE 26

"COLIFORM" GROUP MENINGITIS

Name	Type	Age	Stay in Hospital	Result
Colin F.	Paracolon Bac.	12 days	13 weeks	Gross M.D.; Spastic.
Raymond F.	Paracolon Bac.	15 days	9 weeks	Normal child.
Ian W.	Salmonella Typhii Murium	19 days	3 days	Norml child.
David S.	E. coli	3 days	5 weeks	Normal child

The commonest presenting signs in these 4 patients were anorexia and fever. One only had bulging fontanelle, another neck stiffness, and the one who became grossly mentally retarded had a convulsion shortly after admission. The 2 patients with "paracolon bacillus" infection were twins, and a similar organism was isolated from their stool culture. McKay and Smith (1958)

have reported fully on these patients.

The twins were both treated with a combination of streptomycin, sulphonamide and chloromycetin. Colin's course lasted 42 days and Raymond's for 32 days. Both had steroid therapy. David S. had a six days' course of penicillin, sulphonamide and streptomycin; Ian M. had penicillin for 3 days and chloromycetin for 1 day.

The duration of symptoms prior to admission was 24 hours in the twins, and 48 hours and 72 hours in the others respectively.

The time till the temperature fell to normal was 48 hours in one, 168 hours in the case of the twins, and the remaining patient remained afebrile throughout.

Conclusion:

There are too few cases in this group to draw any conclusion, but it would appear that convulsions may be an indication of a severe infection.

Incidence of convulsions/coma

The following tables show the incidence of convulsions and/or coma related to the type of meningitis on admission in the uncomplicated and complicated groups.

TABLE 27

MENINGOCOCCAL MENINGITIS.

Group	Number of Cases	Convulsions/ Coma	Percentage
Uncomplicated	104	20	19%
Complicated	12	5	42%
Total	116	25	21%

TABLE 28

UNIDENTIFIED MENINGITIS

Group	Number of Cases	Convulsions/ Coma	Percentage
Uncomplicated	61	10	16%
Complicated	18	5	28%
Total	79	15	19%

TABLE 29

PNEUMOCOCCAL MENINGITIS

Group	Number of cases	Convulsions/ Coma	Percentage
Uncomplicated	20	6	30%
Complicated	6	4	67%
Total	26	10	38%

TABLE 30

INFLUENZAL MENINGITIS

Group	Number of Cases	Convulsions/ Coma	Percentage
Uncomplicated	14	3	21%
Complicated	7	3	43%
Total	21	6	28%

TABLE 31

MIXED MENINGITIS

Group	Number of Cases	Convulsions/ Coma	Percentage
Uncomplicated	5	1	20%
Complicated	-	-	-

TABLE 32

COLIFORM MENINGITIS

Group	Number of Cases	Convulsions/ Coma	Percentage
Uncomplicated	3	-	-
Complicated	1	1	100%
Total	4	1	

It can be seen that in each of the four main types of meningitis there is a significant increase in the incidence of convulsions or coma on admission in the complicated group. This is particularly so in the pneumococcal and influenzal infections where the figures were 67% and 43% respectively. This was almost twice the incidence of the uncomplicated pneumococcal and un/complicated influenzal groups.

There was not such a striking difference in the meningococcal and unidentified groups where the figures were complicated:uncomplicated 42%:19% and 28%:16% respectively.

There were not sufficient numbers in the "mixed" or coliform groups for any comment to be worthwhile.

Conclusions:

It would appear that the presence of coma and/or convulsions on admission may suggest that the patient may develop late manifestations of the type reported. Any patients exhibiting convulsions and/or coma on admission should be followed up for several years.

CELL COUNT

It was decided to see if the cell count in the various types of meningitis could be helpful in seeing if there was any marked difference in the complicated and uncomplicated groups.

TABLE 33

MENINGOCOCCAL

	Under 1,000	1-10,000	11-20,000	21-40,000
Complicated	18% (2)	54%(6)	18%(2)	9%(1)
Uncomplicated	20%(15)	62%(41)	17%(13)	7%(5)

Although the number of cases is not many, (indicated in brackets) it can be seen that there is a great similarity in both groups. In the main the majority had less than 10,000 cells

UNIDENTIFIED

	Under 1,000	1-10,000	11-20,000	21-40,000
Complicated	23%(4)	52%(9)	23%(4)	-
Uncomplicated	22%(13)	62%(36)	14%(8)	2%(1)

The numbers are small but the distribution is very similar. Once again the majority had less than 10,000 cells.

PNEUMOCOCCAL

	Under 1,000	1-10,000	11-20,000	21-40,000
Complicated	20%(1)	40%(2)	40%(2)	
Uncomplicated	42%(8)	58%(11)		

This group is much too small for any comparison.

INFLUENZAL

	Under 1,000	1-10,000	11-20,000	21-40,000
Complicated	33%(1)	33%(2)	33%(1)	
Uncomplicated	22%(2)	55%(5)	22%(2)	

The numbers here are probably too small to make any comment.

MIXED GROUP

	Under 1,000	1-10,000	11-20,000	21-40,000
Uncomplicated	1			

COLIFORM GROUP

	Under 1,000	1-10,000	11-20,000	21-40,000
Complicated		1		
Uncomplicated	1			1

No comment can be offered here as once again the figures are too small

Conclusions:

The cell count does not seem to be of help in forecasting which patient is likely to develop late manifestations.

TABLE 34

Age at Onset of Disease.

MENINGOCOCCAL

	0-3 mths	4-6 mths	7-12 mths	1-2 yrs	3-5 yrs	6-12 yrs	Over 12 yrs	Total
Complicated	1	5	2	-	3	1	-	12
Uncomplicated	4	15	36	32	7	10	-	104
Total	5	20	38	32	10	11	-	116

In this type of meningitis 8 of 63 patients developed late manifestations in the under - 12 months age group, an incidence of 12.7%. The other 4 were spread over the next eleven years when there were 53 patients; an incidence of 7.5%

In this type of infection it would seem that there is a relationship between age at onset and the subsequent development of late manifestations. There were 54.3% of the patients in the age group under 12 months, and 45.7% between the age of 1 year and 12 years. It would seem, then, that the younger the age at onset the greater the chance of late manifestations developing.

TABLE 35

AGE AT ONSET OF DISEASE.

UNIDENTIFIED

	0-3 mths	4-6 mths	7-12 mths	1-2 yrs	3-5 yrs	6-12 yrs	Over 12 yrs	Total
Complicated	-	2	2	4	3	7	-	18
Uncomplicated	-	6	12	20	11	11	1	61
Total	-	8	14	24	14	18	1	79

There were 22 patients under the age of 12 months of whom 4 developed late manifestations, an incidence of 17.1%. From the age of 1 - 12 years there were 57 patients of whom 14 developed late manifestations, an incidence of 24.5%.

It would appear that in the unidentified type it is the older age group that has the greater chance of developing late manifestations.

TABLE 36

AGE AT ONSET OF DISEASE

INFLUENZAL

	0-3 mths	4-6 mths	7-12 mths	1-2 yrs	3-5 yrs	6-12 yrs	Over 12 yrs	Total
Complicated	-	-	6	1	-	-	-	7
Uncomplicated	-	-	2	10	1	1	-	14
Total	-	-	8	11	1	1	-	21

In this type of meningitis there were 8 cases under the age of 12 months and six of them developed late manifestations, an incidence of 75%. In the age group 1-12 years there were 13 patients, of whom one developed sequelae, an incidence of 7.7%. Of the total number of patients, 38% were under the age of 12 months and 61% between the age of 1 year and 12 years. It would appear that here the earlier the onset the likelier the chance of late manifestations developing.

TABLE 37

AGE AT ONSET OF DISEASE

PNEUMOCOCCAL

	0-3 mths	4-6 mths	7-12 mths	1-2 yrs	3-5 yrs	6-12 yrs	Over 12 yrs	Total
Complicated	1	-	-	2	-	3	-	6
Uncomplicated	1	2	5	4	-	8	-	20
Total	2	2	5	6	-	11	-	26

In pneumococcal meningitis there were 9 patients under the age of 12 months, and one of these showed late manifestations, an incidence of 11.1% There were 17 patients between the ages of 1 year and 12 years of whom 5 developed sequelae, an incidence of 29.5%. Of the total number of patients 34.6% were under 12 months and 65.3% between 1 year and 12 years. It would appear that the earlier the age at onset does not have a bearing on the subsequent development of late manifestations.

TABLE 38

AGE AT ONSET OF DISEASE

MIXED

	0-3 mths	4-6 mths	7-12 mths	1-2 yrs	3-5 yrs	6-12 yrs	Over 12 yrs	Total
Complicated	-	-	-	-	-	-	-	-
Uncomplicated	-	1	1	-	2	1	-	5
Total	-	1	1	-	2	1	-	5

In this type of meningitis there were no cases who developed late manifestations.

TABLE 39.

AGE AT ONSET OF DISEASE

COLIFORM

	0-3 mths	4-6 mths	7-12 mths	1-2 yrs	3-5 yrs	6-12 yrs	Over 12 yrs	Total
Complicated	1	-	-	-	-	-	-	1
Uncomplicated	3	-	-	-	-	-	-	3
Total	4	-	-	-	-	-	-	4

In the coliform type of meningitis there were too few patients to draw any conclusions.

Conclusions:

There seems to be a relationship between the age at onset and the subsequent development of late manifestations in the meningococcal and influenzal types of infection. No such relationship appears in the unidentified and pneumococcal groups. There were too few cases in the coliform and mixed groups for any observation to be raised.

TABLE 40

Type of Organism causing Meningitis

Type of Meningitis	Complicated	Total number	Percentage
Meningococcal	12	116	10%
Unidentified	18	79	22%
Influenzal	7	21	33%
Pneumococcal	6	26	23%
Mixed	-	5	-
Coliform	1	4	25%
Total	44	251	17%

It can be seen from the above table that influenzal meningitis was the type showing the highest percentage of patients who developed late manifestations, namely 33%. Pneumococcal with 23% and unidentified with 22% were the next most frequent. The figure for the coliform group was too small for comment.

The average percentage for the group as a whole was 17% and the lowest incidence of late manifestations occurred in the meningococcal type of infection, being 10%.

Conclusion:

There is a relationship between the type of organism causing meningitis and the subsequent development of late manifestations. It would appear that influenzal infection gives the highest incidence followed by pneumococcal and unidentified type. The lowest incidence occurred in meningococcal infections.

Summary of Findings:

Duration of symptoms prior to admission.

Of the four main types of meningitis, the duration of symptoms prior to admission did not play a part in the development of late manifestations except in the influenzal variety.

Age at onset of illness. The younger the age of the patient at onset of illness appeared to be significant in the meningococcal and influenzal forms of meningitis but not in the unidentified and pneumococcal varieties.

Time till temperature became normal. In all four main types the time till temperature became normal appeared to play a part in the development of late manifestations.

Duration of stay in hospital. With the exception of the unidentified variety the duration of stay in hospital would appear to be of significance.

Cell count. The cell count was of no importance in all four main types.

Convulsions and coma. There appears to be a higher incidence of both convulsions and/or coma in all four main types of meningitis.

Types of organisms causing meningitis.

Late manifestations occurred in all four main types of meningitis with the highest incidence in the influenzal variety followed in order by pneumococcal, unidentified and meningococcal infections.

DISCUSSION

CONCLUSIONS and SUMMARY.

D I S C U S S I O N.

From the results of this thesis and as reported in the literature, deaths from the common types of purulent meningitis are falling. Despite this gratifying state of affairs there are many children left with severe brain damage. As the majority of children suffering from purulent meningitis occur in the pre-school age group, regular and repeated follow-up is necessary. It has been stressed that maximum therapy rather than minimum should be employed and commenced at the earliest possible moment.

The present work is confined to the North-East of Scotland. It would be interesting to know what the number of brain damaged children following purulent meningitis was in other parts of Great Britain, and how they had been treated during their illness. The size of the problem could be ascertained by having a national survey including a controlled therapeutic trial.

The study of trends over time i.e. the epidemiology of purulent meningitis could be seen from such a survey. In the present work the

commonest forms of purulent meningitis are meningococcal and unidentified types accounting for nearly three quarters of the total. There has been no marked increase in the influenzal type which is often reported as causing the greatest number of brain damaged children, and which is the commonest form found in the United States of America. There is a downward trend in the number of cases in the last four year period covered by this thesis. A national survey would give the picture for the whole country.

The limitations of the present report have been mentioned, and in the future follow-up of patients after purulent meningitis the help and co-operation of School Health and Psychiatric services would be invaluable. A prospective study could be planned when heredity and environmental factors could be explored. In the present series it has been impossible to assess the role of these two most important factors. In several instances the case reports have mentioned a bad family history and in others the children have had a poor environment.

The fact that the child had a severe illness at an early age and subsequently showed impairment of intellect or other similar sequelae is suggestive of a relationship to that illness. This relationship is the more likely as in a severe illness like purulent meningitis the inflammatory process is probably not limited to the meninges but also affects the brain. As has been shown many of the sequelae are of the nature of brain damage e.g. poor concentration span, behaviour problems and impairment of intellect. These symptoms are not apparent immediately after the illness and may be ascertained by regular follow-up or not until after the child has started school.

If an 'at-risk' register was kept the magnitude of the problem could be ascertained both locally and nationally. This would allow plans to be made for the education and psychiatric management of such patients.

CONCLUSIONS AND SUMMARY.

The first section of this thesis gave a factual account of 287 children suffering from acute purulent meningitis occurring in the North-East of Scotland from 1946 - 1961. The commonest form of meningitis was meningococcal followed by the unidentified group. These two types of meningitis account for 209 (73%) of the total number. There were 31 due to pneumococcal infection, 26 to influenzal infection, 12 to coliform organisms and 9 to a mixed group. The age, sex and seasonal distributions are discussed.

The second section showed that of the 251 followed-up, 44 showed sequelae, an incidence of 17%. Many had more than one symptom suggesting brain damage. The site of this damage could not be specified but certainly suggested extension beyond the meninges. Several factors could have been responsible for this brain damage. The age at onset of illness was considered to be important. Environment and heredity factors could not be excluded in the assessment of those who developed sequelae.

There was an overall mortality of 12.5%.

The third section attempted to prove that the patients showing late manifestations of their illness suffered a severe illness. This was based on the longer time taken for the temperature to fall to normal, the longer duration of stay in hospital and the increased incidence of convulsions or coma at the time of admission. The types of therapy used are discussed.

A brief discussion is given suggesting the need for further work, including possibly a National Survey and controlled therapeutic trial. The epidemiology of purulent meningitis requires further study. It is suggested that the co-operation of the School Medical and Psychiatric Services is required to arrange follow-up programmes by having, for example, an 'at risk' register.

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